1.0 Title Page

Clinical Study Protocol M16-244

A Phase 2 Single-Arm Open-Label Extension Study to Investigate Safety with Risankizumab in Psoriatic Arthritis Subjects Who Have Completed Week 24 Visit of Study 1311.5

Incorporating Administrative Change 1 and Amendment 1

AbbVie Investigational Product:	Risankizumab/ABBV-066/previously BI655066
Date:	23 May 2018
Development Phase:	2
Study Design:	This is a single-arm, open-label extension study.
EudraCT Number:	2016-003113-94
Investigator(s):	Multicenter Study: Investigator information is on file at AbbVie.
Sponsor:	For EU Countries:* AbbVie Deutschland GmbH & Co. KG (AbbVie) Knollstrasse 50 67061 Ludwigshafen Germany For Non-EU Countries: AbbVie 1 North Waukegan Road Bldg. AP31 North Chicago, IL 60064 USA
Sponsor Contact:	[redacted]

Emergency Medical Contact:	[redacted]

* The specific contact details of the AbbVie legal/regulatory entity (person) within the relevant country are provided within the clinical trial agreement with the Investigator/Institution and in the Clinical Trial Application with the Competent Authority.

This study will be conducted in compliance with the protocol, Good Clinical Practice and all other applicable regulatory requirements, including the archiving of essential documents.

1.1 Protocol Amendment: Summary of Changes

Previous Protocol Versions

Protocol	Date
Original	29 August 2016
Administrative Change 1	20 March 2017

The purpose of this amendment is to:

- Include changes made as a result of Administrative Change 1.
- Revise inclusion and exclusion criteria to require that women of childbearing potential use contraception throughout the study, including 20 weeks after the last dose of study drug, and exclude subjects who are pregnant, breastfeeding or considering becoming pregnant throughout the study, including 20 weeks after the last dose of study drug.

  Rationale: *Due to additional data clarifying an extension of the risankizumab ($t_{1/2}$) from 16 to 20 weeks in the risankizumab Investigator's Brochure Edition 3.0.*
- Incorporate addition of a follow-up phone call 20 weeks after last dose of study drug.

  Rationale: *Due to additional data clarifying the risankizumab $t_{1/2}$ from 16 to 20 weeks in the risankizumab Investigator's Brochure Edition 3.0.*
- Extend the adverse event (AE) collection period and contraception requirement duration from 16 weeks after the last dose of study drug to 20 weeks after the last dose of study drug.

  Rationale: *Due to additional data clarifying the risankizumab $t_{1/2}$ from 16 to 20 weeks in the risankizumab Investigator's Brochure Edition 3.0.*
- Correct errors in Section 5.4.1 and Appendix J.
- Update information for study contacts in Section 7.0 and Appendix D.

An itemized list of all changes made to this protocol under this amendment can be found in Appendix V.

1.2 Synopsis

AbbVie Inc.	**Protocol Number:** M16-244
Name of Study Drug: Risankizumab/ABBV-066 (previously known as BI 655066)	**Phase of Development:** 2
Name of Active Ingredient: Risankizumab/ABBV-066	**Date of Protocol Synopsis:** 23 May 2018
Protocol Title: A Phase 2, Single-Arm, Open-Label Extension Study to Investigate the Safety with Risankizumab in Psoriatic Arthritis Subjects Who Have Completed Week 24 Visit of Study 1311.5	
Objectives: • Primary objective: o Assess the safety and tolerability of risankizumab in psoriatic arthritis (PsA) subjects who have completed all doses of study drug and Week 24 visit of Study 1311.5 • Secondary objectives: o Assess the efficacy of risankizumab in PsA subjects who have completed all doses of study drug and Week 24 visit of Study 1311.5. o Assess the impact of risankizumab on the inhibition of structural progression in PsA subjects who have completed all doses of study drug and Week 24 visit of Study 1311.5.	
Investigators: Multicenter	
Study Sites: Approximately 70 sites globally	
Study Population: Adult female and male PsA subjects who have completed all doses of study drug and the Week 24 visit of Study 1311.5, and who have met all of the specified inclusion and none of the exclusion criteria.	
Number of Subjects to be Enrolled: Up to 180 subjects will be enrolled in this OLE study.	
Methodology: This is a 52-week multicenter, single-arm, open-label extension (OLE) study to assess the efficacy, safety and tolerability of risankizumab in PsA subjects who have completed all doses of study drug and Week 24 visit of Study 1311.5 (Phase 2 randomized control trial in PsA subjects, sponsored by Boehringer Ingelheim). The subjects may finish Week 24 visit of Study 1311.5 and take the first dose of Study M16-244 on the same day or Study M16-244 start may be delayed up to 8 weeks if needed. All subjects will be on risankizumab 150 mg by subcutaneous injection every 12 weeks (q12w) starting at Week 0 for 36 weeks in an open-label fashion. An additional dose of risankizumab 150 mg by subcutaneous injection will be made available at the Week 4 visit to subjects who have not achieved a protocol defined response (defined as an improvement in tender and swollen joint count of ≥ 20% compared with the baseline in Study 1311.5) and the investigator believes that this additional dose may be beneficial to the subject.	

Diagnosis and Main Criteria for Inclusion/Exclusion:

Main Inclusion:

1. Subjects who have completed all doses of study drug and Week 24 visit of Study 1311.5.
2. Women of childbearing potential who are sexually active, must agree to use at least one accepted method of contraception throughout the study, including 20 weeks after last dose of study drug is given.
3. Women of childbearing potential must have a negative urine pregnancy test at Baseline (Week 0/V1).
4. Subjects must voluntarily sign and date an informed consent, approved by an Independent Ethics Committee (IEC)/Institutional Review Board (IRB), prior to the initiation of any study specific procedures.
5. Subject is judged to be in good health as determined by the Investigator

Main Exclusion:

1. Female subject who is pregnant, breastfeeding or is considering becoming pregnant during study participation, including 20 weeks after the last dose of study drug is given.
2. Premature discontinuation of the study drug in Study 1311.5 for any reason.
3. Use of a biologic treatment other than risankizumab since first dose of study drug in Study 1311.5.
4. Time elapsed is > 8 weeks since the Week 24 visit in Study 1311.5
5. Active systemic infections during the last 2 weeks (exception: common cold) prior to randomization, as assessed by the investigator.

Investigational Product:	Risankizumab (ABBV-066): 75 mg pre-filled syringe, 90 mg/mL, 0.83 mL dispensed volume, 0.87 mL fill volume.
Doses:	Risankizumab (ABBV-066): 150 mg administered every 12 weeks for 36 weeks
Mode of Administration:	Subcutaneous injection
Reference Therapy:	None (Single-arm, Open-Label Extension)
Duration of Treatment: 36 weeks	

Criteria for Evaluation:

Efficacy:

The baseline as defined in Study 1311.5 will be used to derive the efficacy endpoints in this study.

The following endpoints will be assessed at all measured time points:

- American College of Rheumatology (ACR) 20/50/70 response
- Change in Tender Joint Count (TJC) and Swollen Joint Count (SJC) as compared to Baseline
- Change in Health Assessment Questionnaire – Disability Index (HAQ-DI) as compared to Baseline
- Change in Short Form-36 Health Survey (SF-36) as compared to Baseline
- Change in Dactylitis count as compared to Baseline
- Change in Leeds Dactylitis Index (LDI) as compared to Baseline
- Change in Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index
- Leeds Enthesitis Index (LEI) as compared to Baseline
- Change in Modified Nail Psoriasis Severity Index (mNAPSI) as compared to Baseline
- Change in Physician's Global Assessment of Disease Activity (VAS) (PhGA) as compared to Baseline
- Change in Patient's Assessment of PsA Pain Intensity (VAS) as compared to Baseline
- Change in Patient's Global Assessment of Disease Activity (PtGA) as compared to Baseline
- Change in High sensitivity C-Reactive Protein (hsCRP) as compared to Baseline
- Minimal disease activity (MDA)
- Change in Disease Activity Score in 28 joints using hsCRP(DAS28-hsCRP) as compared to Baseline
- Psoriasis (PsO) endpoints assessed in subjects with a ≥ 3% baseline PsO body surface area (BSA):
  - PASI 75 and PASI 90 response
  - Static Physician Global Assessment (sPGA) clear or almost clear (0 or 1)
- European League Against Rheumatism (EULAR) response
- Change in Psoriatic Arthritis Response Criteria (PsARC) as compared to Baseline
- Presence of dactylitis (yes/no)
- Change in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) as compared to baseline
- Change in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) (in subjects with baseline inflammatory spondylitis, based on investigator judgment, in Study 1311.5) as compared to baseline
- Change in Modified total Sharp Score (mTSS) at Weeks 24 and 48

Criteria for Evaluation (Continued):

Pharmacokinetic and Immunogenicity:

Risankizumab plasma concentrations will be determined. Pharmacokinetics (PK) and anti-drug antibodies (ADA) data may be combined with data from other studies and analyzed using a mixed-effects modeling approach. This analysis will estimate the population central value and the empirical Bayesian estimates of the individual values for risankizumab apparent clearance (CL/F) and volume of distribution (V_{ss}/F). Additional parameters may be estimated if useful in the interpretation of the data.

Multiple measurements of ADA for risankizumab will be collected for each subject during the treatment period and the follow-up visit. The percentage of subjects with ADA will be calculated. As appropriate, the effect of ADA on risankizumab PK and efficacy will be explored.

Pharmacodynamic:

Pharmacokinetic/pharmacodynamics relationship will be explored across several clinical laboratory endpoints.

Safety:

Safety and tolerability evaluations include adverse event monitoring, physical examinations, vital sign measurements, and clinical laboratory testing (hematology, chemistry, and urinalysis). Toxicity management guidelines are provided within the study protocol.

Statistical Methods:

Efficacy:

The baseline, as defined in Study 1311.5, will be used to derive the efficacy endpoints in this study.

The proportion of subjects with ACR20/50/70, PASI75/90, sPGA (0/1), EULAR response, presence of dactylitis (yes/no), and MDA (yes/no), will be summarized with 95% confidence intervals by visit and plotted over time.

Change from the baseline will be summarized by visit with descriptive statistics for all continuous variables including each individual component of ACR response (TJC, SJC, PhGA, Patient's Assessment of PsA Pain Intensity, PtGA, HAQ-DI and hsCRP), DAS28-hsCRP, PASI, sPGA, PsARC, Dactylitis Count, LDI, LEI, SPARCC Enthesitis Index, BASDAI mNAPSI, and mTSS using x-ray. Change from baseline will also be summarized by visit with descriptive statistics for measures of quality of life, function and work such as SF-36, and FACIT-F.

Safety:

All subjects who receive at least one dose of risankizumab during the conduct of this study will be included in the safety analysis. Incidence of adverse events, serious adverse events, premature discontinuation, and changes from baseline in vital signs, physical examination results and clinical laboratory values will be analyzed. Treatment-emergent adverse events will be tabulated by Medical Dictionary for Regulatory Activities (MedDRA) system organ class and by Preferred Term (PT). Mean change from baseline, as defined in Study 1311.5 for laboratory and vital signs data will be summarized by visit.

1.3 List of Abbreviations and Definition of Terms

Abbreviations

ACR	American College of Rheumatology
ADA	Anti-Drug Antibody
AE	Adverse Event
AESI	Adverse Event of Special Interest
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
ATEMS	AbbVie Temperature Excursion Management System
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BI	Boehringer Ingelheim
BSA	Body Surface Area
CA	Competent Authority
CCVT	Cardiovascular, Cerebrovascular and Thrombosis
CD	Crohn's Disease
CRA	Clinical Research Associate
DAS28	Disease Activity Score in 28 joints
DILI	Drug Induced Liver Injury
DIP	Distal Interphalangeal
DMARDs	Disease-Modifying Anti-rheumatic Drugs
DMC	Data Monitoring Committee
DN	Double Negative
DNA	Deoxyribonucleic Acid
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
eGFR	Estimated Glomerular Filtration Rate
EOS	End Of Study
EOT	End Of Treatment
EudraCT	European Clinical Trials Database
EULAR	European League Against Rheumatism
FACIT-F	Functional Assessment of Chronic Illness Therapy-Fatigue
FDA	Food and Drug Administration
GCP	Good Clinical Practice

HAQ-DI	Health Assessment Questionnaire-Disability Index
HIV	Human Immunodeficiency Virus
hsCRP	High sensitivity C-Reactive Protein
IB	Investigator's Brochure
IC_{50}	Half-maximal Inhibition
ICH	International Conference on Harmonization
IEC	Independent Ethics Committee
IFN	Interferon
IgG	Immunoglobulin G
IGRA	Interferon Gamma Release Assay
IL	Interleukin
ILCs	Innate Lymphoid Cells
IMP	Investigational Medicinal Product
IP	Investigational Product
IP	Interphalangeal
IRB	Institutional Review Board
IRT	Interactive Response System
ISF	Investigator Site File
i.v.	Intravenous
LDI	Leeds Dactylitis Index
LEI	Leeds Enthesitis Index
mAb	monoclonal Antibody
MACE	Major Adverse Cardiovascular Event
MCP	Metacarpalphalangeal
MDA	Minimal Disease Activity
MedDRA	Medical Dictionary for Regulatory Activities
mNAPSI	Modified Nail Psoriasis Severity Index
MRI	Magnetic Resonance Imaging
mTSS	Modified Total Sharp Score
MTX	Methotrexate
NK	Natural Killer
nM	Nanomolar
NOAEL	No Observed Adverse Effect Level
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs

OMERACT	Outcome Measures in Rheumatology
OLE	Open Label Extension
PASI	Psoriasis Area and Severity Index
PD	Pharmacodynamic
PhGA	Physician's Global Assessment of Disease Activity
PI	Principal Investigator
PIP	Proximal Interpalangeal
PK	Pharmacokinetic
pM	Picomolar
POR	Proof of Receipt
PPD	Purified Protein Derivative
PRN	(Pro re nata) when necessary
PsA	Psoriatic Arthritis
PsARC	Psoriatic Arthritis Response Criteria
PsO	Psoriasis
PT	Preferred Term
PtGA	Patient's Global Assessment of Disease Activity
PUVA	Psoralen and ultraviolet A
RCT	Randomized Control Trial
RCTC	Rheumatology Common Toxicity Criteria
REP	Residual Effect Period
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
s.c.	subcutaneous
SF-36	Short Form-36 Health Survey
SJC	Swollen Joint Count(s)
SPARCC	Spondyloarthritis Research Consortium of Canada
sPGA	Static Physician Global Assessment
SOC	System Organ Class
$t_{1/2}$	Half-life
SUSAR	Suspected Unexpected Serious Adverse Reaction
TB	Tuberculosis
TEAE	Treatment Emergent Adverse Events
TJC	Tender Joint Count(s)

TNF	Tumor necrosis factor
TNFi	Tumor necrosis factor inhibitor(s)
UV(A/B)	Ultraviolet (A/B)
VAS	Visual Analog Scale
W	Week
WBC	White Blood Count
WOCBP	Women of child-bearing potential

Pharmacokinetic and Statistical Abbreviations

AUC	Area under the plasma concentration-time curve
CL/F	Apparent clearance
C_{max}	Maximum observed plasma concentration
C_{trough}	Trough concentration
LOCF	Last observation carried forward
NRI	Non-responder imputation
OC	Observed cases
T_{max}	Time to maximum observed plasma concentration
V_{ss}/F	Volume of distribution

2.0 Table of Contents

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3.0 Introduction

3.1 Medical Background

Psoriatic Arthritis (PsA) is a chronic seronegative spondyloarthritis characterized by peripheral synovitis, enthesitis, dactylitis and spondylitis.[12,24] PsA is mostly associated with Psoriasis (PsO) and nail involvement.[18] Prevalence estimates for PsA among PsO patients vary across studies, ranging from 6 to 30%,[15,16] with PsA affecting about 0.3 to 1% of the global population, equally across men and women.[18] The cause of PsA is not known, but hereditary factors, infection and physical trauma are frequently referred to as potential risk factors.

Although effective treatments for PsA are approved (traditional disease-modifying antirheumatic drugs (DMARDs) (e.g., methotrexate (MTX), leflunomide), apremilast, tumor necrosis factor inhibitors (TNFi) (certolizumab pegol, adalimumab, etanercept, infliximab, golimumab), anti-IL-12/23p40 (ustekinumab), and anti-IL-17 (secukinumab), the unmet medical need remains for safer therapy that works more effectively on measures of signs and symptoms of PsA and prevention of structural damage. Maintenance of efficacy over time, preferably with a new mode of action to provide more treatment options to patients who have already failed the currently approved therapies, is desirable.

Risankizumab is a humanized monoclonal antibody (mAb) directed against human Interleukin 23 (IL-23) that specifically neutralizes this cytokine and prevents binding and signaling through the IL-23 receptor, expressed on T helper 17 cells (T_H17) cells as well as subset of γδ T cells, natural killer (NK) cells, innate lymphoid cells (ILCs) and double negative (DN) entheseal-residing T cells. Risankizumab has a potential for addressing some of the unmet needs in PsA.

PsO and PsA share common pathologies based on cellular pathways (T cells/plasmacytoid dendritic cells), transcription factors (decreased AP-1), genetic susceptibility loci (CARD15/PSORAS1/NOD2, TNF gene polymorphism) and cytokines/other mediators

(TNF, type 1 interferon, amphiregulin).[20] Pro-inflammatory mediators that act as drivers of PsO and PsA are released by a variety of cell types, including innate immune cells, adaptive immune cells and resident immune cells.[9] Plasmacytoid dendritic cells are found in psoriatic skin and psoriatic synovium and activated dendritic cells present antigens and produce interferon (IFN)-α and pro-inflammatory mediators, such as IL-12 and IL-23. Antigen presented by myeloid dendritic cells to T-cells results in proliferation and differentiation into type 1 and type 17 T helper cells, which increase secretion of inflammatory cytokines.[9,21]

The role of the IL-23/IL-17 axis in PsA is well documented in the literature.[13] IL-23 is expressed in the synovial tissue of patients with PsA.[17] Single nucleotide polymorphisms in this genetic pathway are related to genetic susceptibility to PsA.[14,22] IL-23 has been shown to cause enthesitis (one of the key features of PsA) in a rodent model.[10] The role of IL-23 (through its effect on T_H17 cells) has been implied in bone erosion and dysregulated bone formation in PsA. IL-17 can cause cartilage degradation via effects on chondrocytes.[23] In addition, IL-23 (independent of T_H17) activates IL-23R+ entheseal resident lymphocyte cell population, which produces IL-22, and can promote entheseal and periosteal bone formation.[10]

3.2 Drug Profile

Risankizumab is a humanized monoclonal antibody (mAb) of the IgG1 subclass directed towards IL-23p19. The antibody has been engineered to reduce Fcγ receptor and complement binding, and potential charge heterogeneity. Risankizumab binds with high affinity to human IL-23 and inhibits IL-23 stimulated IL-17 production at IC_{50} concentrations below 10 pM, as compared with 167 pM for ustekinumab in the same system. Risankizumab does not affect IL-12 at a maximum tested concentration (33 nM) and it does not inhibit IL-12 stimulated IFN-γ production.

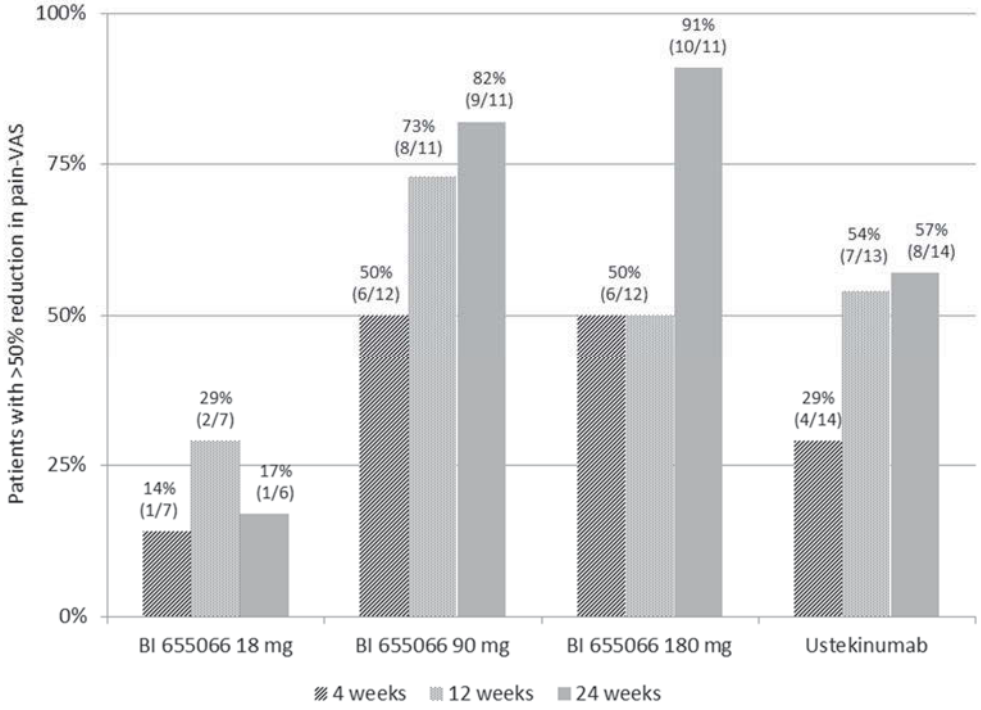
The toxicology data suggest risankizumab can be safely administered to humans, as supported by chronic administration to monkeys for up to 26 weeks. The monkey was identified as the most relevant toxicology species with a NOAEL (no observed adverse

effect level) of 50 mg/kg/dose (highest tested dose), corresponding to an exposure (combined sex) of 677 µg/mL for the C_{max} and 86,250 µg•h/mL for AUC_{0-168}, respectively.

Proof of clinical concept for risankizumab through IL-23/IL-17 pathway was demonstrated in a single rising dose Phase 1 trial in 39 subjects with moderate to severe plaque PsO where 87% of subjects achieved at least 75% reduction in Psoriasis Area and Severity Index (PASI 75) with no safety concerns.[37]

In a Phase 2 dose-ranging trial of risankizumab vs. ustekinumab, the primary endpoint of PASI 90 response at Week 12 was achieved by 32.6% (14/43), 73.2% (30/41), and 81.0% (34/42) of risankizumab subjects in the 18 (single dose at Week 0), 90, and 180 mg (dosed at Weeks 0, 4 and 16) groups, respectively, and 40.0% (16/40) of ustekinumab subjects (dosed at Weeks 0, 4 and 16, weight based). A two-sided Cochran-Mantel-Haenszel test of PASI 90 response at Week 12 between the 18, 90, and 180 mg groups of risankizumab, and ustekinumab, gave p-values of 0.4337, 0.0013, and < 0.0001, respectively.[38] In addition, in this PsO trial, Pain Visual Analog Scale (pain-VAS [0 – 100 mm]) data over time was obtained from 46 subjects who had concurrently diagnosed PsA by a rheumatologist or suspected PsA. The criterion of > 50% decrease in pain-VAS (defined post hoc, as one of the potential domains contributing to ACR 50 response) at Week 24 was achieved in 16.7% (1/6), 81.8% (9/11), and 90.9% (10/11) of subjects on risankizumab18, 90, and 180 mg dose groups, respectively, compared with 57.1% (8/14) for ustekinumab. In the risankizumab 90 and 180 mg dose arms the reductions in pain-VAS score were observed as early as 4 weeks, and were highest at 24 weeks (Figure 1), supporting the therapeutic rationale of risankizumab in PsA. Risankizumab was well tolerated in this Phase 2 study.

Figure 1. Reduction in Pain – Rates of Subjects with > 50% Reduction in Pain-VAS Score from Baseline at Weeks 4, 12, and 24



BI655066 = risankizumab

After a single intravenous (i.v.) administration, risankizumab geometric mean $AUC_{0\text{-inf}}$ ranged from 2.93 – 1650 day•µg/mL and C_{max} from 0.311 – 110 µg/mL, with exposure increasing in a dose-proportional manner. Group mean clearance and terminal phase volume of distribution were 0.33 L/day and 10.8 L, respectively. PK parameter variability, expressed as gCV (%) was < 50%. After a single subcutaneous administration of risankizumab, maximal exposures were reached between 5 – 13 days and subcutaneous bioavailability was 73% (expressed as the ratio of geometric mean dose normalized $AUC_{0\text{-inf}}$ after subcutaneous and i.v. administration).

For a more detailed description of the drug profile refer to the current Investigator's Brochure.[36]

3.3 Differences Statement

Study M16-244 is a 52 week multicenter, single-arm, open-label extension (OLE), consisting of 36 weeks of study drug administration and 20 weeks follow-up, to Study 1311.5. This is the first study to explore safety and efficacy of risankizumab in subjects diagnosed with PsA over this extended duration.

3.4 Benefits and Risks

Participation in this study may generate data to support future use of risankizumab in larger groups of PsA patients. Risankizumab has been studied in 46 PsO Phase 2 Study 1311.2 subjects who had a diagnosis by a rheumatologist, or were suspected by an investigator, of also having PsA. The rates of subjects with a > 50% reduction in pain-VAS at Week 24 (from baseline) in the 90 mg and 180 mg of risankizumab arms were comparable with the ustekinumab arm and numerically better than in the risankizumab 18 mg single dose arm. In addition, 70 – 80% of subjects with moderate to severe PsO receiving 90 mg and 180 mg of risankizumab achieved PASI 90 in their skin disease.

Individual subjects, completing all doses of study drug and the Week 24 visit of Study 1311.5, whose response may benefit or be maintained as a result of increased or exposure of risankizumab will be offered the opportunity to enroll in the OLE.

Subjects who have not achieved a protocol defined response (defined as an improvement in tender and swollen joint count of ≥ 20% compared with the baseline in Study 1311.5) at Week 4 in the OLE trial will be offered an additional dose of risankizumab (150 mg subcutaneous), provided the investigator believes this may be beneficial to the subject. If subjects have not attained a protocol defined response at 2 consecutive visits at Week 12 visit, or thereafter, they will be discontinued from the OLE study. Other criteria leading to discontinuation of individual subjects in this trial are described in Section 5.4.1.

As of March 2016, 546 adult subjects have received at least 1 dose of risankizumab in all completed and ongoing studies. Unblinded safety data (at least up to completion of

randomized treatment period) are available on 465 subjects with PsO, Crohn's disease (CD) or ankylosing spondylitis, 358 of whom received risankizumab.

In the Phase 2 psoriasis trial (Study 1311.2), 126 subjects received risankizumab and the most commonly occurring AEs were nasopharyngitis (32%), headache (9%), back pain (6%), and arthralgia (5%). In the Phase 2 CD trial (Study 1311.6), 82 subjects received risankizumab within the 12 weeks of the randomized treatment period and most frequent AEs were arthralgia (15%), nausea (13%), headache (12%), abdominal pain (11%), vomiting (6%), asthenia (6%), diarrhea (5%), pyrexia (5%), back pain (5%), dizziness (5%), and insomnia (5%). In the Phase 2 ankylosing spondylitis trial (Study 1311.8), 119 subjects received risankizumab during the placebo-controlled period of 12 weeks and the most commonly reported adverse events were nasopharyngitis (12%), headache (10%), fatigue (6%), diarrhea (5%), back pain (5%), and influenza (4%). There was no relationship between treatment groups or doses and the overall frequency of AEs or the occurrence of AEs in specific organ classes, or any individual AE based on available unblinded safety data.

As with any biologic therapy, hypersensitivity reactions may be possible. Local reactions following subcutaneous administration of risankizumab were uncommon, and limited to redness, swelling or induration at the injection site. As with any immune modulating agent, risankizumab may impair immune function resulting in a risk of infection. This will be monitored by collection of any AEs during the treatment and observation periods. There is not enough information at this time to rule out a risk of cancer with risankizumab, but this risk is considered small with this type of compound as experience with the anti-IL-12/23 mAb ustekinumab has not suggested significant risk for cancer/serious infection. Subjects will be monitored for signs and symptoms of malignancy at each visit.

A cardiovascular, cerebrovascular, and thrombosis (CCVT) adjudication committee has been established for comprehensive assessment of this risk. All possible major adverse cardiac event (MACE) and thrombotic events will be adjudicated and overall safety across

all indications will continue to be assessed by a risankizumab independent data monitoring committee.

For periodic updates on rare SAEs and the overall drug safety profile please refer to the current Investigator's Brochure.[36]

Anti-drug antibody (ADA) response was measured in the 24-week trial period in single ascending dose Study 1311.1 with SC and IV administration. None of the subjects in the SC dose group tested positive. From the IV dose group, 6 out of 18 subjects were ADA positive. Four out of these 6 subjects had positive ADA response in their pre-dose samples and only 2 subjects had treatment emergent ADAs-not associated with any ADA-specific AEs. A neutralizing antibody assay was developed and implemented for subsequent trials. In the Phase 2 psoriasis trial (Study 1311.2), treatment-emergent ADAs were detected in 13.7% of subjects receiving risankizumab (17 of 124 patients evaluated). In most subjects these were transient and/or low titer (< 32). Neutralizing ADAs were observed in 3 subjects in the multiple dose risankizumab groups.

4.0 Study Objective

4.1 Primary Objective

The primary objective of Study M16-244 is to assess the safety and tolerability of risankizumab in PsA subjects who have completed all doses of study drug and the Week 24 visit in Study 1311.5.

4.2 Secondary Objectives

Secondary objectives include the assessment of efficacy of risankizumab and the impact of risankizumab on the inhibition of structural progression in PsA subjects who completed all doses of study drug and the Week 24 visit in Study 1311.5.

5.0 Investigational Plan

5.1 Overall Study Design and Plan: Description

This is a 52-week multicenter, single-arm, OLE study to assess safety, tolerability and efficacy of risankizumab in PsA subjects who have completed all doses of study drug and the Week 24 visit of Study 1311.5 (Phase 2 randomized clinical trial in PsA subjects, sponsored by Boehringer Ingelheim).

Subjects who complete all doses of study drug and the Week 24 visit in Study 1311.5, meet all inclusion criteria (Section 5.2.1) and none of the exclusion criteria (Section 5.2.2) have the option to sign the informed consent form and enter the OLE study, receiving risankizumab 150 mg administered every 12 weeks with an additional dose of rizankizumab made available at the Week 4 visit for those subjects that have not achieved a protocol defined response (defined as an improvement in tender and swollen joint count of ≥ 20% compared with the baseline in Study 1311.5), provided the investigator believes this may be beneficial to the subject.

If the Study M16-244 Week 0 visit occurs on the same day or in the 4 days following the Study 1311.5 Week 24 visit only selected activities are required as some activities are common to both studies and are not required twice. See Study Activity Table in Appendix C. If the OLE Week 0 visit occurs > 4 days and ≤ 8 weeks after the Study 1311.5 Week 24 visit, all procedures specified in Appendix C at Week 0 visit are required.

Subjects that enroll in the OLE study are no longer enrolled in Study 1311.5 and will not complete the Week 28 or Week 32 visits in Study 1311.5.

Subjects who are not enrolled in Study M16-244 within 8 weeks of the Study 1311.5 Week 24 visit are not eligible to participate in Study M16-244.

The study is anticipated to enroll up to 180 subjects. Study visits will occur at Week 0/Enrollment, Weeks 4, 12, 24, 36, 48 and 52. A ± 4 day window is permitted around scheduled study visits after enrollment.

36-Week Treatment Period

Administration of study drug will occur at Week 0, 12, 24 and 36, with an additional dose of rizankizumab made available at the Week 4 visit for those subjects that have not achieved a protocol defined response (defined as an improvement in tender and swollen joint count of ≥ 20% compared with the baseline in Study 1311.5), provided the investigator believes this may be beneficial to the subject. Subjects who have not attained a protocol defined response at 2 consecutive visits at Week 12 visit or thereafter, will be discontinued from the OLE study. Other criteria leading to discontinuation of individual subjects in this trial are described in Section 5.4.1.

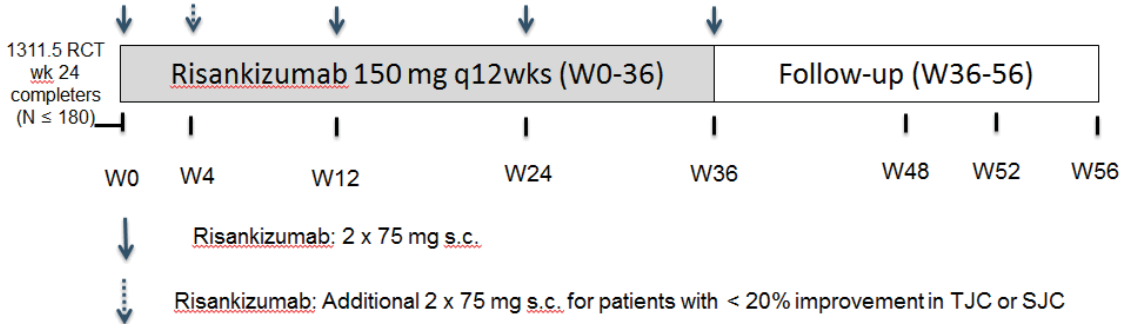
A ± 4-day window is permitted around scheduled study visits after enrollment. If any visit has to be rescheduled, subsequent visits should follow the original visit date schedule.

Follow-Up Period

Subjects will have follow-up visits at Week 48 and 52 and a Follow-up Phone call 20 weeks after the last dose of study drug. All Follow-up Visit procedures are noted in Appendix C. Subjects who discontinue study drug treatment early will need to attend an early End of Treatment (EOT) visit ideally within 2 weeks after the decision and preferably prior to the administration of any new therapies. An End of Study (EOS) visit 16 weeks after the last dose of study drug and a Follow-up Phone Call 20 weeks after the last dose of study drug is required to determine the status of any ongoing AEs/SAEs or the occurrence of any new AEs/SAEs (see Appendix C and Section 5.4.1).

A schematic of the study design is shown below in Figure 2.

Figure 2. Study M16-244 Study Design



5.2 Selection of Study Population

5.2.1 Inclusion Criteria

1. Subjects who have completed all doses of study drug and Week 24 visit of Study 1311.5.
2. Women of childbearing potential must agree to use at least one of the following methods of contraception throughout the study including 20 weeks after the last study drug dose is given.
    - combined (estrogen and progestogen containing) hormonal birth control (oral, intravaginal, transdermal) associated with inhibition of ovulation initiated at least 1 month prior to study participation.
    - progestogen-only hormonal birth control (oral, injectable, implantable) associated with inhibition of ovulation initiated at least 1 month prior to study participation.
    - bilateral tubal occlusion/ligation
    - intrauterine device (IUD)
    - intrauterine hormone-releasing system (IUS).
    - Vasectomized sexual partner(s) (the vasectomized partner(s) should have received medical assessment of the surgical success and is the sole sexual partner of the trial participant).

- True abstinence: Refraining from heterosexual intercourse when this is in line with the preferred and usual lifestyle of the subject (periodic abstinence [e.g., calendar, ovulation, symptothermal, post-ovulation methods] and withdrawal are not acceptable).

Women of childbearing potential are defined as having experienced menarche and are:

- not postmenopausal (12 months with no menses without an alternative medical cause) and are
- not permanently sterilized (e.g., hysterectomy, bilateral oophorectomy or bilateral salpingectomy).

3. Women of childbearing potential must have a negative urine pregnancy test at Baseline (Week 0/V1).
4. Subjects must voluntarily sign and date an informed consent, approved by an Independent Ethics Committee (IEC)/Institutional Review Board (IRB), prior to the initiation of any study specific procedures.
5. Subject is judged to be in good health as determined by the Investigator.

See Appendix D for inclusion criterion specific to France.

Rationale for the Inclusion Criteria:

1, 5	To select the adequate subject population
2, 3	The impact of risankizumab on pregnancy and reproduction is unknown
4	In accordance with harmonized Good Clinical Practice (GCP)

5.2.2 Exclusion Criteria

A subject will not be eligible for study participation if he/she meets any of the following criteria:

1. Female subject who is pregnant, breastfeeding or is considering becoming pregnant during study participation, including 20 weeks after the last dose of study drug is given.
2. Premature discontinuation of study drug in Study 1311.5 for any reason.
3. Use of a biologic treatment other than risankizumab since first dose of study drug in Study 1311.5.
4. Time elapsed is > 8 weeks since the Week 24 visit in Study 1311.5.
5. Active systemic infections during the last 2 weeks (exception: common cold) prior to randomization, as assessed by the investigator.
6. Anticipated requirement during the study or receipt of any live or attenuated vaccine since first dose administered in Study 1311.5.
7. Participation in another investigational study since first dose of study drug in Study 1311.5.
8. Current diagnosis of a major chronic inflammatory or connective tissue disease other than PsA (e.g., rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, Lyme disease, gout) and fibromyalgia as assessed by the Investigator.
9. Use of any restricted medication as specified in this protocol or any drug considered likely to interfere with the safe conduct of the study, as assessed by the investigator, since first dose of study drug in Study 1311.5.
10. History of allergy/hypersensitivity to a systemically administered biologic agent or its excipients.
11. Chronic or relevant acute infections including HIV (human immunodeficiency virus), viral hepatitis and (or) active tuberculosis.
12. Any documented active or suspected malignancy or history of malignancy since first dose of study drug in Study 1311.5, except appropriately treated basal or squamous cell carcinoma of the skin or in situ carcinoma of uterine cervix.

13. Major surgery (including weight loss surgery), performed since first dose of study drug in Study 1311.5 or planned while study is ongoing as assessed by the investigator.

14. Evidence of a current or previous disease, medical condition (including chronic alcohol or drug abuse) other than PsA and PsO, surgical procedure (i.e., organ transplant), medical examination finding (including vital signs and electrocardiogram (ECG)), or laboratory value in Study 1311.5 outside the reference range that in the opinion of the investigator is clinically significant and would make the study participant unreliable to adhere to this protocol or to complete this trial, compromise the safety of the subject, compromise the quality of the data or for any reason cause the Principal Investigator (PI) to consider the subject an unsuitable candidate.

See Appendix D for inclusion criterion specific to France.

Rationale for Exclusion Criteria:

1	The impact of risankizumab on pregnancy and reproduction is unknown
2, 4, 8, 14	To select the adequate subject population
3, 5, 6, 7, 9 – 13	To ensure the safety of the subjects throughout the study

5.2.3 Prior and Concomitant Therapy

Any medication or vaccine (including over-the-counter or prescription medicines, vitamins and/or herbal supplements) that the subject is receiving at the time of enrollment, or receives during the study, must be recorded along with the reason for use, date(s) of administration including start and end dates, and dosage information including dose, route and frequency on the appropriate electronic case report form (eCRF).

The AbbVie Emergency Medical Contact should be contacted if there are any questions regarding concomitant or prior therapy(ies).

5.2.3.1 Prior Therapy

Use of a biologic treatment is prohibited other than risankizumab since initiation in Study 1311.5.

Intra-articular corticosteroids are not permitted within the 4 weeks preceding enrollment and throughout the duration of Study M16-244.

5.2.3.2 Concomitant Therapy

Any medication or vaccines (including over-the-counter or prescription medicines, vitamins and/or herbal supplements) that the subject is receiving since Week 24 of Study 1311.5 and during the study, must be recorded along with the reason for use, date(s) of administration including start and end dates, and dosage information including dose, route and frequency on the appropriate eCRF. The following therapies are allowed for concomitant use:

Methotrexate

Any subjects taking MTX (up to 25 mg/week) must be on a stable dose and stable route of administration for at least 4 weeks before enrollment and ideally maintain this dose throughout the study. Reduction in the dose of MTX will be allowed if the subject can no longer tolerate their dose of MTX.

Folic Acid

Subjects on MTX must be taking folic acid supplementation according to local standard of care before enrollment and during the trial to minimize the likelihood of MTX associated toxicity.

Corticosteroids

Treatment with systemic corticosteroids is permitted up to a maximum daily dosage equivalent to prednisone ≤ 10 mg and if the dose was stable within the 2 weeks preceding enrolment. The subject should remain on a stable dose throughout the study.

Topical steroids of US class 6 (mild, such as desonide) or US class 7 (least potent, such as hydrocortisone) (see list in Appendix T) will be permitted for use limited to the face, axilla, and/or genitalia. These topical medications should not be used within approximately 24 hours prior to a visit.

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) or Paracetamol/Acetaminophen PRN

Stable doses of non-steroidal anti-inflammatory drugs (NSAIDs), cyclooxygenase (COX) 2 inhibitors, or Paracetamol/Acetaminophens are allowed throughout the study. Subjects taking NSAIDs should be advised not to take NSAIDs at least 24 hours prior to study visit. Substitution with another NSAID is permitted over the study duration.

Paper diaries will be provided to subjects to record NSAID, COX-2 inhibitors or Paracetamol/Acetaminophen use throughout the Study M16-244.

Vitamin D

If the subject is taking vitamin D supplements, the subject should continue on stable doses throughout the duration of the trial.

Topical therapy

During the course of the study, subjects may continue treatment with medicated shampoos that do not contain corticosteroids, or bland (without beta or alpha hydroxy acids) emollients. Application of these topical therapies for psoriasis, however, should not occur within 24 hours of a study visit.

5.2.3.3 Prohibited Therapy

Use of the following therapies is prohibited from administration of the first dose of study drug in Study 1311.5 throughout the duration of Study M16-244, including any gap between these two studies:

- Investigational products not otherwise described below

- anti-IL-12/23, and anti-IL-17 agents, including ustekinumab and secukinumab
- Cell-depleting therapies including but not limited to anti-CD20 (e.g., rituximab), investigational agents (e.g., CAMPATH, anti-CD4, anti-CD5, anti-CD3, anti-CD19)
- TNF inhibitors
- JAK inhibitor, Apremilast and leflunomide
- Intra-articular injections (including steroids)
- Intramuscular or intravenous corticosteroid treatment
- Topical PsO treatments such as retinoids, Vitamin A analogs, anthralin and steroids except as permitted in Section 5.2.3.2: Concomitant Therapy
- Oral or injectable PsO medications (not biologicals) including retinoids and fumarates, or any other drugs known to possibly benefit PsO
- Photochemotherapy (e.g., PUVA)
- Any drug known to interfere with or to aggravate PsO including but not limited to lithium and interferons
- Phototherapy (e.g., UVA, UVB)
- Low and high potency opioid analgesics (e.g., methadone, hydromorphone, morphine)
- Live or attenuated vaccines

5.2.4 Contraception Recommendations and Pregnancy

Female subjects of childbearing potential must be ready and able to use highly effective methods of birth control per International Conference on Harmonization (ICH) M3 (R2) that result in a low failure rate of less than 1% per year when used consistently and correctly. Or subjects must have only vasectomized sexual partner(s) or be abstinent. The method chosen must be practiced throughout the study including 20 weeks after the last dose of study drug is given.

Women of childbearing potential are defined as having experienced menarche and are:

- not postmenopausal (12 months with no menses without an alternative medical cause)
- not permanently sterilized (e.g., hysterectomy, bilateral oophorectomy or bilateral salpingectomy).

The following is a list of accepted contraception methods.

- combined (estrogen and progestogen containing) hormonal (oral, intravaginal, transdermal) birth control associated with inhibition of ovulation initiated at least 1 month prior to study participation
- progestogen-only hormonal birth control (oral, injectable, implantable) associated with inhibition of ovulation initiated at least 1 month prior to study participation
- intrauterine device (IUD)
- intrauterine hormone-releasing system (IUS).
- Vasectomized sexual partner(s) (the vasectomized partner should have received medical assessment of the surgical success and is the sole sexual partner of the trial participant).
- True abstinence: Refraining from heterosexual intercourse when this is in line with the preferred and usual lifestyle of the subject (periodic abstinence [e.g., calendar, ovulation, symptothermal, post-ovulation methods] and withdrawal are not acceptable).

In addition, both female subjects of childbearing potential and male subjects with female partners of childbearing potential, taking MTX as background medication, must follow the national regulatory guidelines regarding contraception while taking these medications.

See Pregnancy Testing paragraph in Section 5.3.1.1 for pregnancy testing instructions.

See Appendix D for contraception instructions specific to France.

5.3 Efficacy and Safety Assessments/Variables

5.3.1 Efficacy and Safety Measurements Assessed

Study procedures described are listed in the following section of this protocol and are summarized in tabular format in Appendix C.

5.3.1.1 Study Procedures

Study procedures will be performed at the study visits as specified in Appendix C. Study visits are scheduled at Week 0/Enrollment, Week 4, 12, 24, 36, 48 and 52. Study procedures are discussed in detail in this section, with the exception of drug concentration measurements and antibody measurements (discussed in Section 5.3.2), study drug administration (discussed in Section 5.5.1), and the collection of adverse event (AE) information (discussed in Section 6.1.5). All study data will be recorded in source documents and on the appropriate eCRFs.

Informed Consent

The subject will sign and date a study specific, Independent Ethics Committee (IEC)/Institutional Review Board (IRB) approved, informed consent form before any study specific procedures are performed in order to participate in this study. Details regarding how informed consent will be obtained and documented are provided in Section 9.3.

Inclusion/Exclusion Criteria

Subjects will be evaluated to ensure they meet all inclusion criteria and have none of the exclusion criteria at the Week 0 visit.

Medical and Surgical History

Transcribe medical history from Study 1311.5 source documents and record any updates to represent the status of the Medical and Surgical History at the Week 0 visit.

Demographics

The subject's demographic data, including date of birth, gender, race, and ethnicity will be collected.

Physical Examination

A complete or targeted physical examination will be performed at the designated study visits as specified in Appendix C. A complete physical examination will include vital sign assessment and general appearance as well as evaluation of all organ systems. Targeted physical examination will include vital sign assessment and evaluation of organ systems associated with AE(s) symptoms or laboratory abnormalities. Clinically relevant abnormal findings will be reported as baseline conditions or AEs.

All physical examination findings whether related to an AE or part of a subject's medical history will be recorded on the appropriate eCRF page. For subjects rolling over from Study 1311.5 to the OLE, adverse events ending prior to completion of Study M16-244 ICF will be recorded in preceding Study 1311.5. Abnormalities assessed by the Investigator after the subject has completed the informed consent process of Study M16-244 will be recorded in the eCRFs of Study M16-244.

Vital Signs

Vital signs evaluations will be performed at visits as shown in Appendix C.

This includes temperature, pulse rate, systolic/diastolic blood pressure and respiratory rate. Respiratory rate, pulse rate, and blood pressure will be measured after subjects have been sitting comfortably for at least 5 minutes. Measurement of vital signs should precede blood sampling to avoid the impact of blood sampling on the vital measurements.

12-Lead Electrocardiogram (ECG)

The 12-lead ECGs will be performed as scheduled in Appendix C.

ECGs will be recorded after the subjects have rested for at least 5 minutes in a supine position and will always precede blood sampling. Six limb leads, as specified by Einthoven (I, II and III) and Goldberger (aVR, aVL, aVF), and six pre-cordial leads (V1 – V6), according to Wilson, will be used.

ECGs may be repeated for quality reasons and the repeat used for analysis. Additional ECGs may be collected for safety reasons at the Investigator's discretion. Clinically relevant, abnormal findings will be reported as AEs.

The electronic version of the ECG is regarded as source data. Dated and signed printouts will be stored in the subject's medical file.

Pregnancy Testing

Women of non-childbearing potential (either postmenopausal or permanently surgically sterile as defined in Section 5.2.4) at Baseline in Study M16-244 do not require pregnancy testing.

For women of childbearing potential, as defined in Section 5.2.4 a urine pregnancy test will be done locally prior to enrollment at Day 1 (Week 0) and prior to dosing (where applicable) at each subsequent visit. The urine pregnancy test must be negative for the dosing to occur. If a urine pregnancy test is positive or a subject reports being pregnant during the study, the subject must stop dosing, and have blood drawn for a serum pregnancy test that will be analyzed at the central laboratory. If the serum pregnancy test is positive, dosing must be stopped and the subject must follow the discontinuation procedure described in Section 5.4.1.

At each visit, the study staff should review the pregnancy avoidance recommendations with each subject of childbearing potential and document this discussion in the subject's source records.

X-Ray Assessments

The modified Total Sharp Score (mTSS) method, including distal interphalangeal joints, will be used to evaluate radiographic evidence of damage.[1] X-rays of hands, wrists and feet will be performed at two time points (Weeks 24 and 48, detailed in Appendix C). Images will be read centrally for each subject in a random order and without knowledge of time point, or subject identity, or treatment assignment in Study 1311.5. Subjects who prematurely discontinue from study drug will not be required to collect x-rays at each designated time point, unless they received a dose within the 16 weeks prior to the scheduled time point.

See Appendix D for instructions specific to Germany.

Clinical Laboratory Tests

Subject will be instructed in advance to attend study visits in a fasted state (8 hours no food and only water). If a patient comes in non-fasted where a fasting condition is required, the visit should be performed, the non-fasted condition documented on the laboratory requisition, and the patient reminded about the expected conditions.

Blood samples will be obtained for the laboratory tests listed in Table 1 at the specified time points noted in Appendix C depending on the subject's status in the study. Blood draws should be performed after all clinical assessments and patient reported outcomes, ECGs, and vital sign determinations are obtained before study drug administration during a visit.

Urine samples will be obtained for urinalysis testing at the specified time points as listed in Table 1 and at the time points noted in Appendix C. The central laboratory will be responsible for performing a macroscopic urinalysis (urine dipstick) on the collected urine specimens. Specified abnormal macroscopic urinalyses will be followed up with a microscopic analysis at the central laboratory.

A certified central laboratory will be utilized to process and provide results for the clinical laboratory tests. All abnormal laboratory tests that are considered clinically significant by the investigator will be followed to a satisfactory resolution. Laboratory abnormalities are considered to be adverse events only if they result in discontinuation from the study, necessitate therapeutic medical intervention, and/or if the Investigator considers them to be an adverse event.

Instructions regarding the collection, processing and shipping of these samples will be provided by the central laboratory chosen for this study.

Table 1. Clinical Laboratory Tests

Category	Test Name
Hematology	Hematocrit (Hct) Hemoglobin (Hb) Red Blood Cell Count/Erythrocytes Reticulocyte Count White Blood Cells/Leukocytes Platelet Count/Thrombocytes
Diff. Automatic	Neutrophils (relative count) Eosinophils (relative count) Basophils (relative count) Monocytes (relative count) Lymphocytes (relative count)
Diff. Manual (if Diff Automatic is abnormal)	Neutrophils, bands (Stabs) Neutrophils, polymorphonuclear (PMN) Eosinophils Basophils Monocytes Lymphocytes
Coagulation	Partial Thromboplastin Time (aPTT) Prothrombin time (INR) Fibrinogen
Enzymes	AST (GOT) ALT (GPT) Alkaline Phosphatase (AP) Creatine Kinase (CK) CK-MB, only if CK is elevated Gamma-Glutamyl Transferase (GGT/γ-GT) Lactic Dehydrogenase (LDH) Amylase Lipase
Electrolytes	Calcium Sodium Potassium Chloride Bicarbonate

Table 1. Clinical Laboratory Tests (Continued)

Category	Test Name
Substrates	Glucose BUN (blood urea nitrogen) Uric acid Creatinine eGFR Bilirubin Total Bilirubin Direct (if total is elevated) Bilirubin Indirect (if total is elevated) Troponin (Reflex, in case of elevated CK) Protein, Total Albumin C-Reactive Protein (CRP) (high sensitivity) Cholesterol, total Triglycerides LDL-Cholesterol HDL-Cholesterol
Urine Pregnancy test (only for women of childbearing potential) tested locally	Human Chorionic Gonadotropin in urine
Serum Pregnancy test (only if urine pregnancy test is positive)	Human Serum Chorionic Gonadotropin
Tuberculosis Screen	TB Skin Test (tested locally) or QuantiFERON®-TB Gold
Urinalysis (dipstick)	Urine Nitrite Urine Protein Urine Glucose Urine Ketone Urobilinogen Urine Bilirubin Urine RBC/Erythrocytes Urine WBC/Leukocytes Urine pH Urine creatinine

Table 1. Clinical Laboratory Tests (Continued)

Category	Test name
Urine-Sediment (microscopic examination, only if urinalysis abnormal)	Urine Sediment Bacteria Urine Cast in Sediment Urine Squamous Epithelial Cells Urine Sed. Crys., Unspecified Urine Sediment RBC/Erythrocytes Urine Sediment WBC/Leucocytes

Clinically relevant abnormal findings will be reported as baseline conditions or AE's. A clinically relevant value may be either in- or outside the reference range. Clinically relevant abnormal laboratory test results must be confirmed and should be repeated until normalization or stabilization or until an alternative explanation has been found. Abnormal laboratory values will be also graded for intensity by using RCTC Version 2.0 criteria developed by OMERACT.[11]

See Appendix D for Japan specific requirements.

Tuberculosis Screening

All subjects will be tested for TB by either the QuantiFERON-TB Gold Test (or equivalent) or a TB Skin Test or equivalent, most commonly the Purified Protein Derivative (PPD) at the Week 24 visit. If premature discontinuation occurs prior to Week 24 visit TB testing should occur at EOS visit as specified in Appendix C.

A TB Skin Test or equivalent should be utilized only when a QuantiFERON®-TB Gold Test is not possible for any reason (unless both tests are required per local guidelines).

- QuantiFERON®-TB Gold Test will be analyzed by the central laboratory (QuantiFERON test is preferred over TB Skin Test).
- If the QuantiFERON®-TB Gold Test is NOT possible (or if both the QuantiFERON®-TB Gold Test and the PPD Skin Test are required per local guidelines) the PPD Skin Test will be performed according to standard clinical practice.

- The PPD Skin Test should be read by a licensed healthcare professional between 48 and 72 hours after administration. A subject who does not return within 72 hours will need to be rescheduled for another skin test.
- The reaction will be measured in millimeters (mm) of induration and induration ≥ 5 mm is considered a positive reaction. The absence of induration will be recorded as "0 mm" not "negative."
- If PPD and/or the QuantiFERON®-TB Gold test (or IGRA equivalent) is positive, or if there is a repeat indeterminate QuantiFERON®-TB Gold test (or IGRA equivalent) upon retesting, subjects may continue in the study if further work up (according to local practice/guidelines) establishes conclusively that the subject has no evidence of active tuberculosis.
- If the subject is diagnosed with active tuberculosis, the subject should not receive any further study drug and follow the premature treatment discontinuation procedure (Early EOT visit) in Section 5.4.1.
- If presence of latent tuberculosis is established, then tuberculosis treatment may be deferred until completion of the trial according to clinical judgment of investigator and local country guidelines and it is also necessary to report it as an adverse event in the source documents and eCRFs.
- If subject is known to have a positive QuantiFERON®-TB Gold or PPD test in Study 1311.5 Screening period do not repeat in this study.
- Subjects who have had an ulcerating reaction to the TB Skin Test in the past should not be re-exposed and should not be tested by a PPD skin test.

In the case of a tuberculosis-related adverse event, a supplemental case report form that provides additional information is to be completed by the investigator or designee.

See Appendix D for TB testing instructions for Japan sites.

Other Safety Parameters

Local Tolerability

Local tolerability at the administration site of the previous subcutaneous injection will be assessed by the investigator according to "swelling," "induration," "heat," "redness,"

"pain," or "other findings" at the specified visits as noted in Appendix C. Any abnormal findings at the injection site during the current visit will be reported as AEs.

Assessments and Patient Reported Outcomes

Clinical and patient reported efficacy endpoints will be assessed over the course of the study at the time points defined in Appendix C. Patient Reported Outcomes (PROs) should be completed by the patient on his/her own in a pre-specified order in a quiet area/room before any other visit assessments or treatments, and, if possible, before any interaction with the investigator or other members of the study team. Details of the following clinical, efficacy and patient reported efficacy assessments are listed in the appendices.

- Tender (68) and Swollen (66) Joint Count
- ACR Response Components
- Dactylitis (LDI)
- Enthesitis (LEI and SPARCC)
- MDA
- DAS28-hsCRP
- EULAR response criteria
- PsARC response
- PASI and sPGA for patients with ≥ 3% BSA of psoriatic plaques at baseline in Study 1311.5 and/or current visit
- mNAPSI
- mTSS

Patient Reported Outcomes

The order of completion should be as follows, applicable for each PRO as specified in Appendix C.

- PtGA

- Patient's Assessment of PsA Pain Intensity (VAS)
- HAQ-DI
- BASDAI – For subjects that presented with inflammatory spondylitis at baseline to Study 1311.5 based on investigator judgment.
- SF-36
- FACIT-F

Study Drug Administration

Refer to Section 5.5.1.

Monitoring for Hypersensitivity Reactions

Subjects should be closely monitored for signs and symptoms of hypersensitivity reactions for approximately 2 hours after the first dose administration (baseline visit) and 1 hour after all other dose administrations at study visits. Hypersensitivity reactions should be treated according to medical standards. Pre-medications for further injections might be considered and will be agreed on between investigator and the AbbVie Medical Director.

In the event of a suspected hypersensitivity reaction or other systemic post-dose reaction, a (PK/ADA) blood and urine sample will be collected once within 24 hours of the reaction.

In the event of a suspected systemic hypersensitivity reaction, a supplemental form that provides additional information is be completed by the investigator or designee.

5.3.2 Drug Concentration Measurements

5.3.2.1 Collection of Samples for Analysis

Blood Samples for Risankizumab Assay

Blood samples for risankizumab assay will be collected at each study visit by venipuncture into appropriately labeled collection tubes. Blood collection will occur after

patient reported outcomes, clinical assessments, ECG, vital signs, and before study drug administration. The time of collection will be recorded to the nearest minute and at the visits specified in Appendix C.

Seven samples will be collected per subject for PK analysis during the treatment and follow-up periods with the potential for one more sample collected in the event of a hypersensitivity reaction.

Blood Samples for Risankizumab Anti-Drug Antibody (ADA) Assay:

Blood samples for risankizumab ADA assay will be collected at each study visit by venipuncture into appropriately labeled collection tubes. Blood collection will occur after questionnaires, clinical assessments, ECG, vital signs, and before study drug administration. The time of collection will be recorded to the nearest minute and at the visits specified in Appendix C.

Seven samples will be collected per subject for ADA analysis during the treatment and follow-up periods with the potential for one more sample collected in the event of a hypersensitivity reaction.

5.3.2.2 Handling/Processing of Samples

Details for the handling and processing of the samples will be provided outside this protocol in the laboratory manual.

5.3.2.3 Disposition of Samples

The frozen plasma samples for risankizumab concentration and risankizumab ADA assays will be packed and shipped from the study site to the Central Laboratory according to instructions in the central laboratory Lab Manual. An inventory of the samples included will accompany the package.

5.3.2.4 Measurement Methods

Plasma concentrations of risankizumab and relative titers of risankizumab ADA will be determined using validated methods under the supervision of the Bioanalysis department at AbbVie. Any additional analytes may be analyzed using non-validated methods. Plasma samples collected for risankizumab and risankizumab ADA analysis may be used for future assay development or validation activities. Risankizumab ADA samples upon request may be used for the analysis of neutralizing anti-drug antibodies.

5.3.3 Efficacy Variables

The baseline as defined in Study 1311.5 will be used to derive the efficacy endpoints in this study.

5.3.3.1 Primary Endpoint(s)

Not applicable.

5.3.3.2 Secondary Endpoint(s)

- ACR 20 response at all measured time points
- Change in mTSS at Week 24 and 48 as compared to baseline

5.3.3.3 Further Endpoint(s)

Further efficacy endpoints will include, but are not limited to, the following:

- ACR 50 at all measured time points
- ACR 70 at all measured time points
- Change in Tender Joint Count at all measured time points as compared to baseline
- Change in Swollen Joint Count at all measured time points as compared to baseline
- Change in HAQ-DI at all measured time points as compared to baseline
- Change in SF-36 at all measured time points as compared to baseline

- Change in Dactylitis count at all measured time points as compared to baseline
- Change in SPARCC Enthesitis Index at all measured time points as compared to baseline
- Change in mNAPSI at all measured time points as compared to baseline
- Change in PhGA (VAS) at all measured time points as compared to baseline
- Change in Patient's Assessment of PsA Pain Intensity (VAS) at all measured time points as compared to baseline
- Change in PtGA assessments at all measured time points as compared to baseline
- Change in High sensitivity C-Reactive Protein (hsCRP) at all measured time points as compared to baseline
- Minimal disease activity (MDA) at all measured time points
- Change in DAS28-hsCRP at all measured time points as compared to baseline
- PsO endpoints assessed at all measured time points in subjects with a ≥ 3% baseline PsO BSA:
  - PASI 75 and PASI 90 response
  - Change in sPGA clear and almost clear
- EULAR (European League Against Rheumatism) response at all measured time points
- Change in PsARC (Psoriatic Arthritis Response Criteria) at all measured time points as compared to baseline
- Presence of dactylitis (yes/no) at all measured time points
- Change in LDI at all measured time points as compared to baseline
- Change in LEI at all measured time points as compared to baseline
- Change in FACIT-F at all measured time points as compared to baseline
- Change in BASDAI at all measured time points (in subjects with baseline inflammatory spondylitis, based on investigator judgment, in Study 1311.5) as compared to baseline

5.3.4 Safety Variables

Safety will be assessed descriptively based on:

- Adverse events*
- Serious adverse events (SAEs)
- Clinical laboratory values (hematology, clinical chemistry and urinalysis)
- Physical examination
- Vital signs
- 12-lead ECG
- Local tolerability

* Intensity of adverse events will be assessed by Rheumatology Common Toxicity Criteria (RCTC) version 2.0 developed by OMERACT.[11]

5.3.5 Pharmacokinetic Variables

Risankizumab plasma concentrations will be determined. PK and ADA data may be combined with data from other studies and analyzed using a mixed-effects modeling approach. This analysis will estimate the population central value and the empirical Bayesian estimates of the individual values for risankizumab apparent clearance (CL/F) and volume of distribution (V_{ss}/F). Additional parameters may be estimated if useful in the interpretation of the data.

5.4 Removal of Subjects from Therapy or Assessment

5.4.1 Discontinuation of Individual Subjects

A subject may withdraw from the study at any time. The Investigator may discontinue any subject's participation for any reason, including an adverse event, safety concerns or failure to comply with this protocol.

Subjects will be withdrawn from the study drug and prematurely discontinued if any of the following occur:

- A subject does not attain a protocol defined response (defined as an improvement in tender and swollen joint count of ≥ 20% compared with the baseline in Study 1311.5) at 2 consecutive visits at Week 12 visit, or thereafter.
- A subject experiences a moderate/grade 2 or above (Rheumatology Common Toxicity Criteria v 2.0) non-serious AE of a systemic hypersensitivity reaction, for which there is no clear alternative explanation.
- A subject experiences a moderate/grade 2 adverse event of vasculitis (Rheumatology Common Toxicity Criteria v 2.0) for which there is no clear alternative explanation.
- Subject experiences severe, grade 3 or greater, or life threatening injection site reaction (ISR) (as defined by the Rheumatology Common Toxicity Criteria v 2.0) which includes prolonged induration, superficial ulceration and includes thrombosis or major ulceration or necrosis requiring surgery.
- A subject has a confirmed platelet count < 50,000 cells/mm^3 (Rheumatology Common Toxicity Criteria v 2.0).
- Clinically significant confirmed abnormal laboratory results or adverse events, which rule out continuation of the study drug, as determined by the Investigator and the AbbVie study designated physician.
- The Investigator believes it is in the best interest of the subject.
- The subject requests withdrawal from the study, and is no longer willing to participate in study procedures or receive contact from the site.
- Inclusion and exclusion criteria violation was noted after the subject started study drug, when continuation of the study drug would place the subject at risk as determined by the AbbVie study designated physician.
- Introduction of prohibited medications or dosages when continuation of the study drug would place the subject at risk as determined by the AbbVie study designated physician.
- The subject becomes pregnant while on study drug.

- Subject is significantly non-compliant with study procedures which would put the subject at risk for continued participation in the trial in consultation with the AbbVie study designated physician.

If, during the course of study drug administration, the subject prematurely discontinues study participation, the procedures outlined for the early EOT visit must be completed, ideally within 2 weeks of the decision and preferably prior to the initiation of another therapy. However, these procedures should not interfere with the initiation of any new treatments or therapeutic modalities that the Investigator feels are necessary to treat the subject's condition. For subjects that prematurely discontinue, study drug will not be given at the early EOT visit and subjects should attend their EOS Visit 16 weeks after last study drug dose and complete a Follow-up Phone Call 20 weeks after the last dose of study drug to determine the status of any ongoing AEs/SAEs or the occurrence of any new AEs/SAEs (see Appendix C).

Subjects who prematurely discontinue from study drug will not be required to collect x-rays at a designated time point, unless they received a dose within the 16 weeks prior to the scheduled time point.

All attempts must be made to determine the primary reason for premature discontinuation. The information will be recorded on the appropriate eCRF page.

For subjects that are considered lost to follow-up, reasonable attempts must be made to obtain information on the final status of the subject. At a minimum, two phone calls must be made and one certified letter must be sent and documented in the subject's source documentation.

Subjects who discontinue the study prematurely will not be replaced.

5.4.2 Discontinuation of Entire Study

AbbVie may terminate this study prematurely, either in its entirety or at any study site, for reasonable cause provided that written notice is submitted in advance of the intended

termination. The investigator may also terminate the study at his/her site for reasonable cause, after providing written notice to AbbVie in advance of the intended termination. Advance notice is not required by either party if the study is stopped due to safety concerns. If AbbVie terminates the study for safety reasons, AbbVie will immediately notify the investigator by telephone and subsequently provide written instructions for study termination.

5.5 Treatments

5.5.1 Treatments Administered

All subjects will receive subcutaneous injections of risankizumab by two 75 mg (150 mg total) pre-filled syringes starting at Week 0 and every 12 weeks thereafter over a 36 week period with a possibility of an additional dose at the Week 4 visit. A subject will be eligible for the additional 150 mg dose at the Week 4 visit if they have not achieved a protocol response (defined as an improvement in tender and swollen joint count of ≥ 20% compared with the baseline in Study 1311.5) and the investigator believes this may be beneficial to the subject.

Risankizumab will be administered as a subcutaneous injection in the abdomen, thighs, gluteal regions, or upper arms (contra-lateral to that used for pharmacokinetic (PK)/pharmacodynamics (PD) samples). The two injections done subsequently should be at least 2 cm apart and should not be close to a vein. The injection sites should avoid sites of psoriasis involvement as well as sites where the skin is tender, bruised, erythematous, or indurated and should be alternated to other areas for subsequent doses. Additional dosing instructions will be provided.

Subjects are to remain at the site to allow the site to monitor for signs and symptoms of hypersensitivity reactions for approximately 2 hours after the dose administered at Week 0 visit and 1 hour following all other doses of study drug (visits after Week 0).

In addition, study personnel administrating the injections should be trained in diagnosing and treating acute allergic reactions, as well as there should be immediate access to medication and equipment to treat such reactions.

5.5.2 Identity of Investigational Product

Information about the risankizumab formulation to be used in this study is presented in Table 2.

Risankizumab supplies will be provided by Boehringer Ingelheim Pharma GmbH & Co KG, Biberach, Germany.

- Risankizumab (ABBV-066) 75 mg/0.83 mL Solution for Injection Pre-filled Syringe

Risankizumab is presented in a 1 mL pre-filled syringe with 0.87 mL of solution for injection. Dispensed volume is 0.83 mL. The solution in the risankizumab syringes has a concentration of 90 mg/mL, to deliver 75 mg per syringe. Two (2) syringes will be used to achieve the 150 mg dose.

Table 2. Identity of Investigational Product

Study Drug	Dosage Form	Strength	Route of Administration	Manufacturer
Risankizumab (ABBV-066)	Solution for injection in pre-filled syringe	75 mg/0.83 mL	Subcutaneous injection	Boehringer Ingelheim Pharma GmbH & Co. KG

5.5.2.1 Packaging and Labeling

Study drug packaged in 75 mg pre-filed syringes will be provided in open-label fashion and packaged in cartons containing one (1) syringe per carton. Each kit will be labeled as required per local requirements. The number of kits dispensed will be managed by the IRT (Interactive Response System).

All labels must remain affixed to the study drug at all times, and should never be removed for any reason.

5.5.2.2 Storage and Disposition of Study Drug(s)

Risankizumab kits will be kept protected from light in their original packaging, in a refrigerator between 2°C to 8°C (36°F to 46°F), and within a secure limited access storage area, and in accordance with the recommended storage conditions on the label. Study medication drug must not be frozen at any time. A temperature log must be maintained for documentation.

The refrigerator temperature must be recorded each business day. Malfunctions or any temperature excursion must be reported to the Sponsor immediately. Study drug should be quarantined and not dispensed until AbbVie or the AbbVie Temperature Excursion Management System (ATEMS) deems the drug as acceptable.

All clinical supplies must be stored and locked in a secure place until they are dispensed for subject use or are returned to AbbVie.

Investigational products are for investigational use only and are to be used only within the context of this study.

5.5.3 Method of Assigning Subjects to Treatment Groups

This is an open-label study. The treatment is the same for all subjects so there is no assignment of subjects to treatment groups.

Study drug will be administered at the study visits summarized in Appendix C.

5.5.4 Selection and Timing of Dose for Each Subject

An IRT will be used to allocate study drug to subjects. At visits where study drug is to be administered, study sites will be required to complete the study drug resupply module in the IRT to receive assigned study drug/kit numbers.

Study drug will be administered at the study site by authorized study personnel (e.g., study nurse).

Injections will be given in an open label fashion with each subject receiving 2 injections of risankizumab (75 mg) at each dosing visit.

Dose modifications or adjustments are not permitted. In exceptional cases of missed or delayed visits, study drug of the following visit should not be administered within 14 days of the prior dose. There should be at least 14 days between two consecutive study drug administrations.

5.5.5 Treatment Compliance

The investigator or his/her designated and qualified representatives will administer study drug only to subjects enrolled in the study in accordance with this protocol. The study drug must not be used for reasons other than that described in this protocol.

5.5.6 Drug Accountability

The investigator and/or named subinvestigators must agree not to supply study drug to any persons not enrolled in the study.

The investigator or representative will verify that study drug supplies are received intact at the appropriate temperature (temperature recording devices [e.g., TempTales] are provided in the shipments), and in the correct amounts from the drug depot.

This will be documented by signing and dating the Proof of Receipt (POR) or similar document included with each drug shipment, and via direct reporting in the IRT. The original POR note or similar document will be kept in the site files as a record of what was received.

An accurate running inventory of study drug will be kept by the site, and will include the kit number, lot number, subject number, Proof of Receipt number(s), the number of pre-

filled syringes dispensed, initials of person who dispensed/administered the drug, and the date study drug was administered for each subject.

All empty Investigational Product boxes and used pre-filled syringes will be inventoried by the site. Each site will use their own sharps disposal container designated to store used pre-filled syringes from the Study M16-244. Empty Investigational Product boxes and sharps containers should be retained by the site for accountability and compliance purposes. Empty Boxes and sharps containers will be retained (unless prohibited by local law) until the CRA is on site to confirm the returned study drug. CRAs and site staff will complete study drug accountability via study drug logs, source documents, subject dosing sheets, empty IP boxes and by visually inspecting the syringes in the sharps container whenever possible. Used sharps containers should never be opened.

An overall accountability of the study drug will be performed and verified by AbbVie monitor throughout the study and at the site close-out visit. After verification of drug accountability, used syringes must be destroyed at the site according to local regulations governing biohazardous waste. Destruction of used study supplies must be documented. All unused supplies must be inventoried, accounted for and destroyed on site according to local procedures or regulation or returned to a destruction facility by the CRA. A copy of the Drug Accountability Form, in accordance with instructions provided by the AbbVie monitor, will be included in the return shipments.

5.6 Discussion and Justification of Study Design

5.6.1 Discussion of Study Design and Choice of Control Groups

Subjects who have completed all doses of study drug and the Week 24 visit of Study 1311.5 and meet all the inclusion criteria and none of the exclusion criteria will be allowed to enroll in the Study M16-244 to receive risankizumab for up to 36 weeks. The primary objective of Study M16-244 is to assess the safety and tolerability of risankizumab in subjects with PsA. All subjects will receive risankizumab 150 mg subcutaneous every 12 weeks in an open-label fashion with the possibility of an additional dose at the Week 4 visit to subjects who have not achieved a protocol defined response

(defined as an improvement in tender and swollen joint count of ≥ 20% compared with the baseline in Study 1311.5) and the investigator believes that this additional dose may be beneficial to the subject.

5.6.2 Appropriateness of Measurements

All efficacy measurements in this study are standard and validated for psoriatic arthritis and/or psoriasis. All clinical and laboratory procedures in this study are standard and generally accepted.

5.6.3 Suitability of Subject Population

This OLE study will enroll subjects who have completed all doses of study drug and Week 24 visit of Study 1311.5. Only those subjects who have met all of the specified inclusion and none of the exclusion criteria will have an option to enter into the OLE study to receive risankizumab, as long as the subject is willing and the Investigator believes that receiving risankizumab is appropriate. The study population selected in this study reflects the standard population for PsA trials with new intervention.

5.6.4 Selection of Doses in the Study

Risankizumab doses of 150 mg subcutaenous administered with different dosing frequencies (every 4 weeks to every 12 weeks) and 75 mg subcutaneous administered as a single dose are currently being evaluated in the Phase 2 study (Study 1311.5) in subjects with psoriatic arthritis. In addition, risankizumab dose of 150 mg subcutaneous administered at Week 0, 4 and then every 12 weeks for up to 104 weeks is currently being evaluated in the Phase 3 studies in subjects with psoriasis. The Phase 2 studies of risankizumab in subjects with psoriasis and CD have evaluated risankizumab doses up to 180 mg subcutaneous administered at Week 0, 4 and then every 12 weeks (in subjects with psoriasis) and up to 600 mg administered intravenously every 4 weeks for up to 26 weeks as induction treatment followed by 180 mg subcutaeous administered every 8 weeks during maintenance period (in subjects with CD).

As of March 2016, 546 adult subjects have received at least 1 dose of risankizumab in all completed and ongoing studies. Unblinded safety data (at least up to completion of randomized treatment period) are available on 465 subjects with PsO, CD and ankylosing spondylitis subjects, 358 of whom received risankizumab.

The doses of risankizumab evaluated in these studies have been found to be well tolerated. There was no relationship between risankizumab dose and the overall frequency of AEs, the occurrence of AEs in specific organ classes, or any individual AE (Risankizumab IB, version 7).

The risankizumab exposures at the dose of 150 mg every 12 weeks to be administered in this study will be covered by the doses administered or currently being administered in other Phase 2 and 3 studies in subjects with psoriasis, psoriatic arthritis and CD. At Week 4 in this study, if a subject has not achieved a protocol defined response (defined as a clinical response is defined as an improvement in tender and swollen joint count of $\geq$ 20% compared with the baseline in Study 1311.5), an additional dose of risankizumab can be administered, provided the investigator believes this may be beneficial to the subject. In summary, this dose has been well tolerated in previous studies with demonstrated efficacy in PsO Phase 2 trials. Some of the subjects treated for PsO also had PsA. The majority of these PsA subjects experienced an improvement in pain-VAS using risankizumab dosed at 0, 4 and 16 weeks. Given the safety and efficacy profile to date, this dose and schedule was chosen.

6.0 Complaints

A Complaint is any written, electronic, or oral communication that alleges deficiencies related to the physical characteristics, identity, quality, purity, potency, durability, reliability, safety, effectiveness, or performance of a product/device after it is released for distribution.

The investigational product in this trial contains both:

- Biologic compound and

- Device component (pre-filled syringe).

Complaints associated with any component of this investigational product must be reported to the Sponsor (Section 6.2.2). For adverse events, please refer to Section 6.1. For product complaints, please refer to Section 6.2.

6.1 Medical Complaints

The investigator will monitor each subject for clinical and laboratory evidence of adverse events on a routine basis throughout the study. The investigator will assess and record any adverse event in detail including the date of onset, event diagnosis (if known) or sign/symptom, severity, time course (end date, ongoing, intermittent), relationship of the adverse event to study drug, and any action(s) taken. For serious adverse events considered as having "no reasonable possibility" of being associated with study drug, the investigator will provide an Other cause of the event. For adverse events to be considered intermittent, the events must be of similar nature and severity. Adverse events, whether in response to a query, observed by site personnel, or reported spontaneously by the subject will be recorded.

All adverse events will be followed to a satisfactory conclusion. Subjects who discontinue for an AE should have careful and regular follow-up in this interval to ensure full resolution of the AE.

6.1.1 Definitions

6.1.1.1 Adverse Event

An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not the event is considered causally related to the use of the product.

Such an event can result from use of the drug as stipulated in protocol or labeling, as well as from accidental or intentional overdose, drug abuse, or drug withdrawal. Any worsening of a pre-existing condition or illness is considered an adverse event. Worsening in severity of a reported adverse event should be reported as a new adverse event. Laboratory abnormalities and changes in vital signs are considered to be adverse events only if they result in discontinuation from the study, necessitate therapeutic medical intervention, and/or if the investigator considers them to be adverse events.

An elective surgery/procedure scheduled to occur during a study will not be considered an adverse event if the surgery/procedure is being performed for a pre-existing condition and the surgery/procedure has been pre-planned prior to study entry. However, if the pre-existing condition deteriorates unexpectedly during the study (e.g., surgery performed earlier than planned), then the deterioration of the condition for which the elective surgery/procedure is being done will be considered an adverse event.

Prior to use, every attempt should be made to contact the AbbVie Study Designated Physician for direction on re-introduction of study drug therapy after prohibited medication administration.

6.1.1.2 Serious Adverse Events

If an adverse event meets any of the following criteria, it is to be reported to AbbVie as a serious adverse event (SAE) within 24 hours of the site being made aware of the serious adverse event.

Death of Subject	An event that results in the death of a subject.
Life-Threatening	An event that, in the opinion of the investigator, would have resulted in immediate fatality if medical intervention had not been taken. This does not include an event that would have been fatal if it had occurred in a more severe form.

Hospitalization or Prolongation of Hospitalization	An event that results in an admission to the hospital for any length of time or prolongs the subject's hospital stay. This does not include an emergency room visit or admission to an outpatient facility.
Congenital Anomaly	An anomaly detected at or after birth, or any anomaly that results in fetal loss.
Persistent or Significant Disability/Incapacity	An event that results in a condition that substantially interferes with the activities of daily living of a study subject. Disability is not intended to include experiences of relatively minor medical significance such as headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (e.g., sprained ankle).
Important Medical Event Requiring Medical or Surgical Intervention to Prevent Serious Outcome	An important medical event that may not be immediately life-threatening or result in death or hospitalization, but based on medical judgment may jeopardize the subject and may require medical or surgical intervention to prevent any of the outcomes listed above (i.e., death of subject, life-threatening, hospitalization, prolongation of hospitalization, congenital anomaly, or persistent or significant disability/incapacity). Additionally, any elective or spontaneous abortion or stillbirth is considered an important medical event. Examples of such events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

For serious adverse events with the outcome of death, the date and cause of death will be recorded on the appropriate case report form.

6.1.1.3 Adverse Events of Special Interest (AESI)

The term AESI relates to any specific AE that has been identified at the compound level as being of particular concern for prospective safety monitoring and safety assessment

within this trial, e.g., the potential for AEs based on knowledge from other compounds in the same class. Ongoing evaluation of adverse events may identify future AESI.

The following are considered as AESI:

Hepatic Injury

A hepatic injury is defined by the following alterations of hepatic laboratory parameters:

- an elevation of AST and/or ALT > 3-fold ULN combined with an elevation of total bilirubin > 2-fold ULN measured in the same blood draw sample, and/or
- marked peak aminotransferase (ALT, and/or AST) elevations ≥ 10-fold ULN.

These lab findings constitute a hepatic injury alert and the subjects showing these lab abnormalities need to be followed up as outlined in the hepatic injury CRF.

In case of clinical symptoms of hepatic injury (icterus, unexplained encephalopathy, unexplained coagulopathy, right upper quadrant abdominal pain, etc.) without lab results (ALT, AST, total bilirubin) available, the investigator should make sure these parameters are analysed, if necessary with an unscheduled blood test. Should the results meet the criteria of hepatic injury alert, investigators are advised to provide a hepatic workup as outline in the hepatic injury CRF.

Study drug should be discontinued if any of the following laboratory values listed below have been confirmed by repeat testing with a new sample:

- ALT or AST > 3 × ULN and (Total bilirubin [TBL] > 2 × ULN or International Normalized Ratio [INR] > 1.5)
- ALT or AST > 3 × ULN with the appearance of fatigue, nausea, vomiting, right upper quadrant pain or tenderness, fever, rash, and/or eosinophilia (> 5%)
- ALT or AST > 8 × ULN
- ALT or AST > 5 × ULN for more than 2 weeks

In the case of a hepatic-related adverse event diagnosed clinically or by laboratory findings, a supplemental case report form that provides additional information will be completed by the investigator or designee.

6.1.2 Adverse Event Severity

Intensity of AEs

The intensity grading of AEs will be performed according to Rheumatology Common Toxicity Criteria (RCTC) Version 2.0 developed by OMERACT.[11] Refer to the Investigator Site File (ISF) for intensity/severity classification. Intensity options are:

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

6.1.3 Relationship to Study Drug

The investigator will use the following definitions to assess the relationship of the adverse event to the use of study drug:

Reasonable Possibility	An adverse event where there is evidence to suggest a causal relationship between the study drug and the adverse event.
No Reasonable Possibility	An adverse event where there is no evidence to suggest a causal relationship between the study drug and the adverse event.

For causality assessments, events assessed as having a reasonable possibility of being related to the study drug will be considered "associated." Events assessed as having no reasonable possibility of being related to study drug will be considered "not associated." In addition, when the investigator has not reported a causality or deemed it not assessable, AbbVie will consider the event associated.

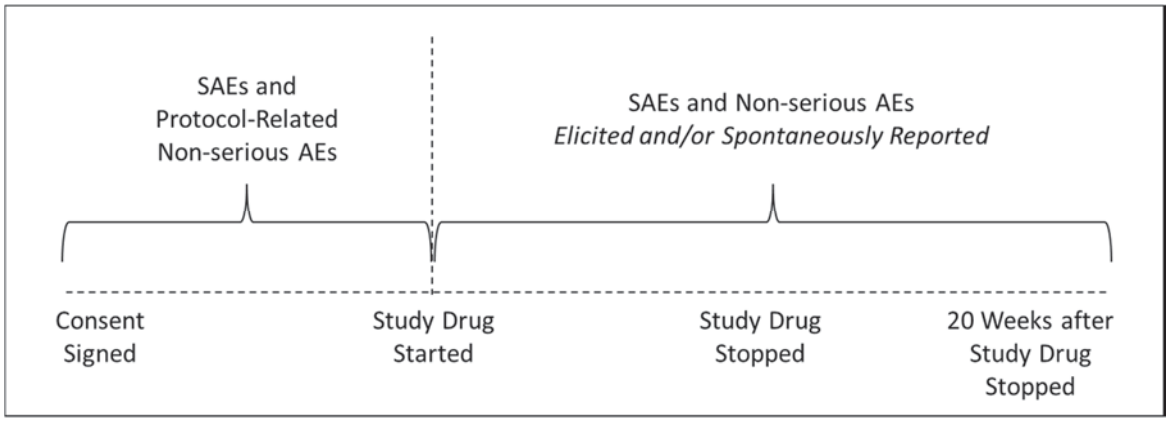
If an investigator's opinion of no reasonable possibility of being related to study drug is given, an Other cause of event must be provided by the investigator for the serious adverse event.

6.1.4 Adverse Event Collection Period

All adverse events reported from the time of study drug administration until 20 weeks, following discontinuation of study drug administration have elapsed will be collected, whether solicited or spontaneously reported by the subject. In addition, serious adverse events and protocol-related non-serious adverse events will be collected from the time the subject signed the study-specific informed consent.

Adverse event information will be collected as shown in Figure 3.

Figure 3. Adverse Event Collection



6.1.5 Adverse Event Reporting

In the event of a serious adverse event, whether associated with study drug or not, the Investigator will notify Clinical Pharmacovigilance within 24 hours of the site being made aware of the serious adverse event by entering the serious adverse event data into the electronic data capture (EDC) system. Serious adverse events that occur prior to the site having access to the RAVE® system, or if RAVE is not operable, should be documented

on the SAE Non-CRF forms and emailed (preferred route) or faxed to Clinical Pharmacovigilance within 24 hours of the site being made aware of the serious adverse event.

Email: [redacted] **FAX to**

For safety concerns, contact the Immunology Safety Team at:

Immunology Safety Team
[redacted]
1 North Waukegan Road
North Chicago, IL 60064
USA

Office:
Email: [redacted]

For any subject safety concerns, please contact the physician listed below:

Primary Therapeutic Area Medical Director:

[redacted]

In emergency situations involving study subjects when the Primary Therapeutic Area Medical Director (TA MD) is not available by phone, please contact the 24-hour AbbVie Medical Escalation Hotline where your call will be re-directed to a designated backup AbbVie TA MD:

24-hour AbbVie Medical Escalation Phone Hotline:
[redacted]

The sponsor will be responsible for Suspected Unexpected Serious Adverse Reactions (SUSAR) reporting for the Investigational Medicinal Product (IMP) in accordance with Directive 2001/20/EC. The reference document used for SUSAR reporting in the EU countries will be the most current version of the Investigator's Brochure.

In Japan, the principal investigator will provide documentation of all serious adverse events to the Director of the investigative site and the Sponsor.

6.1.6 Pregnancy

Pregnancy in a study subject must be reported to AbbVie within 1 working day of the site becoming aware of the pregnancy. Subjects who become pregnant during the study must be discontinued (Section 5.4.1).

Information regarding a pregnancy occurrence in a study subject and the outcome of the pregnancy will be collected.

Pregnancy in a study subject is not considered an adverse event. However, the medical outcome of an elective or spontaneous abortion, stillbirth or congenital anomaly is considered a serious adverse event and must be reported to AbbVie within 24 hours of the site becoming aware of the event.

6.2 Product Complaint

6.2.1 Definition

A Product Complaint is any Complaint (see Section 6.0 for the definition) related to the biologic or drug component of the product or to the medical device component(s).

For a product this may include, but is not limited to, damaged/broken product or packaging, product appearance whose color/markings do not match the labeling, labeling discrepancies/inadequacies in the labeling/instructions (example: printing illegible), missing components/product, device not working properly, or packaging issues.

For medical devices, a product complaint also includes all deaths of a patient using the device, any illness, injury, or adverse event in the proximity of the device, an adverse event that could be a result of using the device, any event needing medical or surgical intervention including hospitalization while using the device and use errors.

Any information available to help in the determination of causality by the device to the events outlined directly above should be captured.

6.2.2 Reporting

Product Complaints concerning the investigational product and/or device must be reported to the Sponsor within 24 hours of the study site's knowledge of the event via the Product Complaint form. Product Complaints occurring during the study will be followed-up to a satisfactory conclusion. All follow-up information is to be reported to the Sponsor (or an authorized representative) and documented in source as required by the Sponsor. Product Complaints associated with adverse events will be reported in the study summary. All other complaints will be monitored on an ongoing basis.

Product Complaints may require return of the product with the alleged complaint condition (syringe). In instances where a return is requested, every effort should be made by the investigator to return the product within 30 days. If returns cannot be

accommodated within 30 days, the site will need to provide justification and an estimated date of return.

The description of the complaint is important for AbbVie in order to enable AbbVie to investigate and determine if any corrective actions are required.

7.0 Protocol Deviations

AbbVie does not allow intentional/prospective deviations from this protocol unless when necessary to eliminate an immediate hazard to study subjects. The principal investigator is responsible for complying with all protocol requirements, and applicable global and local laws regarding protocol deviations. If a protocol deviation occurs (or is identified) after a subject has been enrolled, the principal investigator is responsible for notifying Independent Ethics Committee (IEC)/Institutional Review Board (IRB) regulatory authorities (as applicable), and the following AbbVie Clinical Monitor(s):

Primary Contact: Alternate Contact:

Such contact must be made as soon as possible to permit a review by AbbVie to determine the impact of the deviation on the subject and/or the study.

See Appendix D for Japan specific requirements.

8.0 Statistical Methods and Determination of Sample Size

8.1 Statistical and Analytical Plans

8.1.1 Datasets for Analysis

The analysis set consists of all subjects who enrolled into this OLE study and received at least one dose of open-label study drug. This analysis set will be the primary analysis population for both efficacy and safety analysis.

8.1.2 Subject Accountability

The number of subjects who received at least 1 dose of study drug, the number of subjects who completed the study, and the number of subjects who prematurely discontinued will be summarized overall and by site.

8.1.3 Demographic and Baseline Characteristics

Demographic and baseline disease characteristics endpoints from Study 1311.5 will be summarized descriptively. Summary statistics for continuous variables will include the number of observations, mean, standard deviation, median, Q1, Q3 and range for continuous variables; frequencies and percentages for the discrete variables.

8.1.4 Subject Disposition and Study Drug Exposure

8.1.4.1 Subject Disposition

The number and percentage of subjects who are enrolled and received at least one dose of study drug, and the number of subjects who prematurely discontinued and the reason for premature discontinuation will be summarized. Premature discontinuation of study drug will be summarized with frequencies and percentages overall and by reason for discontinuation for all subjects who received at least one dose of study drug. Subjects may have multiple reasons for prematurely discontinuing study drug, but will be counted no more than once for the total ("Any Reason").

8.1.4.2 Study Drug Exposure

Extent of exposure to study drug will be summarized for all subjects who received at least one dose of study drug in Study M16-244. The duration (days) of study treatment will be summarized with the mean, standard deviation, median, Q1, Q3 and range. The duration of treatment is defined as the difference between the dates of the first and last doses of the treatment plus 1 day.

8.1.5 Efficacy Analysis

The baseline for all efficacy analysis in this study will be the baseline in Study 1311.5.

8.1.5.1 Efficacy Variable

Please see Section 5.3.3 for the list of all efficacy endpoints in this study.

A subject will be considered an ACR20/50/70 responder if compared to the baseline in Study 1311.5.

1. The counts for both SJC (66 joints count) and TJC (68 joints count) have reduced by 20%/50%/70% or more; and
2. At least three of the five remaining ACR core set measures show reduction of 20%/50%/70% or more in:
    a. Patient's Assessment of PsA Pain Intensity (VAS)
    b. Patient's Global Assessment of Disease Activity (PtGA)
    c. Physician's Global Assessment of Disease Activity (PhGA)
    d. Patient's Assessment of Physical Function by Heath Assessment Questionnaire – Disability Index (HAQ-DI)
    e. High sensitivity C-reactive protein

The other efficacy endpoints will be defined in details in Statistical Analysis Plan (SAP).

8.1.5.2 Efficacy Analysis

The efficacy analyses will be conducted with the analysis set described in Section 8.1.1.

For binary endpoints, frequencies and percentages will be calculated with 95% confidence intervals at each post-baseline time point. For the change from baseline measurement, the mean with 95% CI, standard deviation, median, Q1, Q3 and range will be reported at each post-baseline time point.

8.1.5.3 Multiple Comparisons

Not applicable.

8.1.6 Safety Analysis

8.1.6.1 General Considerations

All subjects who receive at least one dose of study drug in this OLE study will be included in the safety analysis.

Incidence of adverse events, serious adverse events, premature discontinuation, and changes in vital signs, physical examination results, and clinical laboratory values will be analyzed for Study M16-244.

Treatment-emergent adverse events (TEAEs) will be tabulated by system organ class (SOC) and Preferred Term (PT).

Mean change from baseline for laboratory and vital signs data will be summarized. Baseline for vital signs, physical examination results, and clinical laboratory results for subjects will be the data collected at the Week 0 visit immediately prior to study drug administration in Study 1311.5.

Missing safety data will not be imputed.

8.1.6.2 Analysis of Adverse Events

8.1.6.2.1 Treatment-Emergent Adverse Events

AEs will be coded using MedDRA. A TEAE is defined as an AE that began or worsened in severity after initiation of study drug. AEs starting more than 140 days following the last dose of study drug will not be included in summaries of TEAEs.

As a general safety summary, the number and percentage of subjects experiencing TEAEs will be summarized for each treatment group for the following AE categories:

- All TEAEs;
- All severe TEAEs;
- All reasonably possibly related TEAEs;
- All SAEs;
- Discontinuations due to TEAEs;
- All TEAEs of special interest
- Death.

Additional TEAEs may be considered for tabulation/summary based on recommendations from Clinical and Safety as deemed appropriate.

TEAEs will be summarized and presented by SOCs and PTs using MedDRA. The SOCs will be presented in alphabetical order, and the

PTs will be presented in alphabetical order within each SOC.

TEAE will also be summarized by maximum severity and by maximum relationship.

The intensity grading of AEs will be performed according to Rheumatology Common Toxicity Criteria (RCTC) Version 2.0 developed by OMERACT.[11] Intensity options are:

Grade 1	mild
Grade 2	moderate

Grade 3	severe
Grade 4	life-threatening

The TEAEs of special interest currently include hepatic injury.

Listing of all SAEs, AEs leading to death, and TEAEs leading to study drug discontinuation and TEAE of special interest will be generated.

8.1.6.2.2 Serious Adverse Events and Death

Deaths and all SAEs will be presented in listing format. In addition, SAEs will be summarized by MedRA SOC and PTs.

8.1.6.3 Analysis of Laboratory and Vital Signs

Changes from baseline in continuous laboratory, vital sign, and ECG parameters will be summarized with the mean, standard deviation and median by visit.

Vital signs and laboratory data will be described by statistical characteristics and frequency of abnormal values. Frequencies and percentages of subjects with laboratory shifts from baseline to the final values using normal ranges to define categories (low, normal, high, and missing) will be summarized by the respective categories. Values beyond the normal values will be listed. Low or high laboratory values will also be flagged in the data listings.

Analysis details will be specified in the Statistical Analysis Plan.

8.1.7 Pharmacokinectic and Exposure-Response Analysis

Individual risankizumab plasma concentrations will be tabulated and summarized with appropriate statistical methods. In addition, ADA titers will be tabulated for each subject at the respective study visits. The percentage of subjects with ADA will be calculated.

Data from this study may be combined with data from other risankizumab studies for the population pharmacokinetic and exposure-response analyses. Population pharmacokinetic

and exposure-response analyses of only data from this study may not be conducted. The following general methodology will be used for the population pharmacokinetic analysis. Population pharmacokinetic analyses of risankizumab will be performed using the actual sampling time relative to dosing. Pharmacokinetic models will be build using a non-linear mixed-effects modeling approach with NONMEM software (Version 7, or a higher version). The structure of the starting pharmacokinetic model will be based on the pharmacokinetic analysis data from previous studies. Apparent CL/F and apparent V_{ss}/F of risankizumab will be the pharmacokinetic parameters of major interest in the NONMEM analyses. If necessary, other parameters, including the parameters describing absorption characteristics, may be estimated if useful in the analysis.

The evaluation criteria described below will be used to examine the performance of different models:

1. The objective function of the best model is significantly smaller than the alternative model(s).
2. The observed and predicted concentrations from the preferred model are more randomly distributed across the line of unity (a straight line with zero intercept and a slope of one) than the alternative model(s).
3. Visual inspection of model fits standard errors of model parameters and change in inter-subject and intra-subject error.

Once an appropriate base pharmacokinetic model (including inter- and intra-subject error structure) is developed, empirical Bayesian estimates of individual model parameters will be calculated by the posterior conditional estimation technique using NONMEM. The relationship between these conditional estimates CL/F and V_{ss}/F values with only potentially physiologically relevant or clinically meaningful covariates (such as ADA class subject age, sex, body weight, concomitant medications, possibly baseline inflammatory and disease markers) will be explored using stepwise forward selection method, or another suitable regression/smoothing method at a significance level of 0.05.

After identification of all relevant covariates, a stepwise backward elimination of covariates from the full model will be employed to evaluate the significance (at $P < 0.005$, corresponding to a decrease in objective function > 7.88 for one degree of freedom) of each covariate in the full model.

In general, all continuous covariates will be entered in the model, initially in a linear fashion, with continuous covariates centered on the median value. Linear or non-linear relationships of primary pharmacokinetic parameters with various covariates may also be explored.

As appropriate, the effect of ADA on risankizumab pharmacokinetics and efficacy will be explored. Relationships between exposure and clinical observations (efficacy or safety variables of interest) may be explored.

8.1.8 Interim Analysis

Not applicable.

8.1.9 Data Monitoring Committee

A data monitoring committee (DMC), independent of the Sponsor will be established to assess the progress of the clinical trials, including safety assessment at specified intervals, and to recommend to the Sponsor whether to continue, modify, or stop the trial. The tasks and responsibilities of the DMC will be specified in the DMC Charter.

8.1.10 CCVT Adjudication Committee

An independent adjudication committee, established for risankizumab development and used in the Study 1311.5 will continue adjudicating all observed cardio- and cerebro-vascular events, and thrombotic events (CCVT) including major adverse cardiovascular events (MACE). The events that are adjudicated and the adjudication process will be detailed in the CCVT Adjudication Committee Charter.

8.2 Determination of Sample Size

Study 1311.5 will enroll approximately 180 subjects. The sample size of Study M16-244 will depend on how many subjects complete all doses of study medication and the Week 24 visit of Study 1311.5 and enroll in this OLE.

9.0 Ethics

9.1 Independent Ethics Committee (IEC) or Institutional Review Board (IRB)

Good Clinical Practice (GCP) requires that the clinical protocol, any protocol amendments, the Investigator's Brochure, the informed consent and all other forms of subject information related to the study (e.g., advertisements used to recruit subjects) and any other necessary documents be reviewed by an Independent Ethics Committee (IEC)/Institutional Review Board (IRB). The IEC/IRB will review the ethical, scientific and medical appropriateness of the study before it is conducted. IEC/IRB approval of the protocol, informed consent and subject information and/or advertising, as relevant, will be obtained prior to the authorization of drug shipment to a study site.

Any amendments to this protocol will require IEC/IRB approval prior to implementation of any changes made to the study design. The investigator will be required to submit, maintain and archive study essential documents according to ICH GCP.

Any serious adverse events that meet the reporting criteria, as dictated by local regulations, will be reported to both responsible Ethics Committees and Regulatory Agencies, as required by local regulations. During the conduct of the study, the investigator should promptly provide written reports (e.g., ICH Expedited Reports, and any additional reports required by local regulations) to the IEC/IRB of any changes that affect the conduct of the study and/or increase the risk to subjects. Written documentation of the submission to the IEC/IRB should also be provided to AbbVie.

9.2 Ethical Conduct of the Study

The study will be conducted in accordance with the protocol, International Conference on Harmonization (ICH) guidelines, applicable regulations and guidelines governing clinical study conduct and the ethical principles that have their origin in the Declaration of Helsinki. Responsibilities of the clinical investigator are specified in Appendix A.

9.3 Subject Information and Consent

The investigator or his/her representative will explain the nature of the study to the subject, and answer all questions regarding this study. Prior to any study-related procedures at the Week 0 visit being performed on the subject, the informed consent statement will be reviewed and signed and dated by the subject, the person who administered the informed consent, and any other signatories according to local requirements. A copy of the informed consent form will be given to the subject and the original will be placed in the subject's medical record. An entry must also be made in the subject's dated source documents to confirm that informed consent was obtained prior to any study-related procedures and that the subject received a signed copy.

Information regarding incentives for subjects and information regarding provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the study can be found in the informed consent form.

9.3.1 Informed Consent Form and Explanatory Material

Prior to the performance of any study specific procedures, including discontinuation of any protocol prohibited medications, the investigator or representative will explain the nature of study procedures and the study to the subject and if applicable per local requirements the subject's legal representative, and all questions regarding the study will be answered. The informed consent form will be reviewed and consent to participate documented by dated signature of the representative and the person administering the informed consent.

See Appendix D for Japan specific requirements.

10.0 Source Documents and Case Report Form Completion

10.1 Source Documents

Source documents are defined as original documents, data and records. This may include hospital records, clinical and office charts, laboratory data/information, subjects' diaries or evaluation checklists, pharmacy dispensing and other records, recorded data from automated instruments, microfiches, photographic negatives, microfilm or magnetic media, and/or x-rays. Data collected during this study must be recorded on the appropriate source documents.

Due to the nature of an open label extension study, data that is common to both Study 1311.5 and Study M16-244 studies may be shared. AbbVie will provide instruction regarding entry of this data.

The investigator(s)/institution(s) will permit study-related monitoring, audits, IEC/IRB review, and regulatory inspection(s), providing direct access to source data documents.

10.2 Case Report Forms

Case report forms (CRF) must be completed for each subject enrolled in this study. These forms will be used to transmit information collected during the study to AbbVie and regulatory authorities, as applicable. The CRF data for this study are being collected with an electronic data capture (EDC) system called Rave® provided by the technology vendor Medidata Solutions Incorporated, NY, USA. The EDC system and the study-specific electronic case report forms (eCRFs) will comply with Title 21 CFR Part 11. The documentation related to the validation of the EDC system is available through the vendor, Medidata, while the validation of the study-specific eCRFs will be conducted by AbbVie and will be maintained in the Trial Master File at AbbVie.

The investigator will document subject data in his/her own subject files. These subject files will serve as source data for the study. All eCRF data required by this protocol will

be recorded by investigative site personnel in the EDC system. All data entered into the eCRF will be supported by source documentation.

The investigator or an authorized member of the investigator's staff will make any necessary corrections to the eCRF. All change information, including the date and person performing the corrections, will be available via the audit trail, which is part of the EDC system. For any correction, a reason for the alteration will be provided. The eCRFs will be reviewed periodically for completeness, legibility, and acceptability by AbbVie personnel (or their representatives). AbbVie (or their representatives) will also be allowed access to all source documents pertinent to the study in order to verify eCRF entries. The principal investigator will review the eCRFs for completeness and accuracy and provide his or her electronic signature and date to eCRFs as evidence thereof.

Medidata will provide access to the EDC system for the duration of the trial through a password-protected method of internet access. Such access will be removed from investigator sites at the end of the site's participation in the study. Data from the EDC system will be archived on appropriate data media (CD-ROM, etc.) and provided to the investigator at that time as a durable record of the site's eCRF data. It will be possible for the investigator to make paper printouts from that media.

Patient Reported Outcome (PRO) data must be completed for each subject enrolled in this study. The subject will enter patient reported data responses on paper CRF provided by AbbVie. Investigative Site personnel will enter the subject's responses from the paper CRFs into the appropriate CRFs in the EDC system. Any corrections to the paper CRFs can only be made by the subject, and will include the date and person (initials) performing the corrections. All changed information in the CRF, including the date and person performing the corrections, will be available via the audit trail, which is the part of the EDC system.

The following PROs will be used in this study:

- SF-36

- BASDAI
- HAQ-DI
- FACIT-F
- PtGA
- Patient Assessment of PsA Pain Intensity (VAS)

11.0 Data Quality Assurance

Computer logic and manual checks will be created to identify items such as inconsistent study dates. Any necessary corrections will be made to the eCRF.

Prior to the initiation of the study, a meeting will be held with AbbVie personnel, the investigators and appropriate site personnel. This meeting will include a detailed discussion of the protocol, performance of study procedures, CRF and Subject Diary completion, and specimen collection methods. The AbbVie monitor will monitor each site throughout the study.

All data hand entered in the database will be verified at AbbVie. Any discrepancies will be reviewed against the CRF and corrected on-line. After completion of the entry process, computer logic checks will be run to check for such items as inconsistent study dates. Any necessary corrections will be made to the database via addenda.

Routine hematology, serum chemistry and serology, and urinalysis will be conducted using a central laboratory. The data from these analyses will be electronically transferred from the central laboratory to the study database.

12.0 Use of Information

All information concerning specify study drug and AbbVie operations, such as AbbVie patent applications, formulas, manufacturing processes, basic scientific data, or formulation information, supplied by AbbVie and not previously published is considered confidential information. The information developed during the conduct of this clinical

study is also considered confidential and will be used by AbbVie in connection with the development of specify study drug. This information may be disclosed as deemed necessary by AbbVie to other clinical investigators, other pharmaceutical companies, and to governmental agencies. To allow for the use of the information derived from this clinical study and to ensure complete and thorough analysis, the investigator is obligated to provide AbbVie with complete test results and all data developed in this study and to provide direct access to source data/documents for trial-related monitoring, audits, IEC/IRB review and regulatory inspection. This confidential information shall remain the sole property of AbbVie, shall not be disclosed to others without the written consent of AbbVie, and shall not be used except in the performance of this study. The investigator will maintain a confidential subject identification code list of all subjects enrolled in the study (by name and subject number). This list will be maintained at the site and will not be retrieved by AbbVie.

13.0 Completion of the Study

The investigator will conduct the study in compliance with this protocol and complete the study within the timeframe specified in the contract between the investigator and AbbVie. Continuation of this study beyond this date must be mutually agreed upon in writing by both the investigator and AbbVie. The investigator will provide a final report to the IEC/IRB following conclusion of the study, and will forward a copy of this report to AbbVie or their representative.

The investigator must retain any records related to the study according to local requirements. If the investigator is not able to retain the records, he/she must notify AbbVie to arrange alternative archiving options.

AbbVie will select the signatory investigator from the investigators who participate in the study. Selection criteria for this investigator will include level of participation as well as significant knowledge of the clinical research, investigational drug and study protocol. The signatory investigator for the study will review and sign the final study report in

accordance with the European Agency for the Evaluation of Medicinal Products (EMEA) Guidance on Investigator's Signature for Study Reports.

The EOS is defined as the date of the last subject's last scheduled visit or the date of the Follow-up Phone Call, whichever is later, see Appendix C.

See Appendix D for Japan specific requirements.

14.0 Investigator's Agreement

1. I have received and reviewed the Investigator's Brochure for risankizumab.
2. I have read this protocol and agree that the study is ethical.
3. I agree to conduct the study as outlined and in accordance with all applicable regulations and guidelines.
4. I agree to maintain the confidentiality of all information received or developed in connection with this protocol.
5. I agree that all electronic signatures will be considered the equivalent of a handwritten signature and will be legally binding.

Protocol Title:	A Phase 2, Single-Arm, Open-Label Extension Study to Investigate the Safety with Risankizumab in Psoriatic Arthritis Subjects Who Have Completed Week 24 Visit of Study 1311.5
Protocol Date:	23 May 2018

Signature of Principal Investigator | Date

Name of Principal Investigator (printed or typed)

15.0 Reference List

15.1 Published References

1. Ware JE, Kosinski M, Keller SD, editors. SF-36 Physical and Mental Health Summary Scales: A User's Manual. 3rd, revised ed. Boston: The Health Institute, New England Medical Center; 1994.
2. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology. Preliminary definition of improvement in rheumatoid arthritis. Arthritis Rheum. 1995;38(6):727-35.
3. Fredriksson T, Pettersson U. Severe psoriasis--oral therapy with a new retinoid. Dermatologica. 1978;157(4):238-44.
4. Ware JE, editor. SF-36 Health Survey: Manual and Interpretation Guide. Boston: The Health Institute, New England Medical Center; 1993.
5. van Gestel AM, Haagsma CJ, van Riel PLCM. Validation of rheumatoid arthritis improvement criteria that include simplified joint counts. Arthritis Rheum. 1998;41(10):1845-50.
6. Mease PJ, Gladman DD, Ritchlin CT, et al. Adalimumab Effectiveness in Psoriatic Arthritis Trial Study Group. Adalimumab for the treatment of patients with moderately to severely active psoriatic arthritis: results of a double-blind, randomized, placebo-controlled trial. Arthritis Rhem. 2005;52(10):3279-89.
7. Yellen SB, Cella DF, Webster K, et al. Measuring fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) measurement system. J Pain Symptom Manage. 1997;13(2);63-74.
8. Webster K, Cella D, Yost K. The Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System: properties, applications, and interpretation. Health Qual Life Outcomes. 2003;1:79.
9. Nestle FO, Kaplan DH, Barker J. Psoriasis. N Engl J Med. 2009;361(5):496-509.

10. Sherlock JP, Joyce-Shaikh B, Turner SP, et al. IL-23 induces spondyloarthropathy by acting on ROR-γt+ CD3+CD4-CD8- entheseal resident T cells. Nat Med. 2012;18(7):1069-76.
11. Woodworth T, Furst DE, Alten R, et al. Standardizing assessment and reporting of adverse effects in rheumatology clinical trials II: the Rheumatology Common Toxicity Criteria v.2.0. J Rheumatol. 2007;34(6):1401-14.
12. Gottlieb A, Korman NJ, Gordon KB, et al. Guidelines of care for the management of PsO and psoriatic arthritis. Section 2. Psoriatic arthritis: overview and guidelines of care for treatment with an emphasis on the biologics. J Am Acad Dermatol. 2008;58(5):851-64.
13. Frleta M, Siebert S, McInnes IB. The interleukin-17 pathway in psoriasis and psoriatic arthritis: disease pathogenesis and possibilities of treatment. Curr Rheumatol Rep. 2014;16(4):414.
14. Filer C, Ho P, Smith RL, et al. Investigation of association of the IL12B and IL23R genes with psoriatic arthritis. Arthritis Rheum. 2008;58(12):3705-09.
15. Zachariae H, Zachariae R, Blomqvist K, et al. Quality of life and prevalence of arthritis reported by 5,795 members of the Nordic PsO Associations. Data from the Nordic Quality of Life Study. Acta Derm Venereol. 2002;82(2):108-13.
16. Prey S, Paul C, Bronsard V, et al. Assessment of the risk of psoriatic arthritis in patients with plaque PsO: a systematic review of the literature. J Eur Acad Dermatol Venereol. 2010;24 (Suppl 2):31-5.
17. Celis R, Planell N, Fernández-Sueiro JL, et al. Synovial cytokine expression in psoriatic arthritis and associations with lymphoid neogenesis and clinical features. Arthritis Res Ther. 2012;14 (2); R93.
18. Gladman DD, Antoni C, Mease P, et al. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. Ann Rheum Dis. 2005;64 Suppl 2:ii14-7.
19. van der Heijde D, Sharp J, Wassenberg S, et al. Psoriatic arthritis imaging: a review of scoring methods. Ann Rheum Dis. 2005;64 (Suppl 2):ii61-4.

20. Ciocon DH, Kimball AB. Psoriasis and psoriatic arthritis: separate or one and the same? Br J Dermatol. 2007;157(5):850-60.

21. Yawalkar N, Tscharner GG, Hunger RE, et al. Increased expression of IL-12p70 and IL-23 by multiple dendritic cell and macrophage subsets in plaque psoriasis. J Dermatol Sci. 2009;54(2):99-105.

22. Liu Y, Helms C, Liao W, et al. A genome-wide association study of psoriasis and psoriatic arthritis identifies new disease loci. PLoS Genet. 2008;4(3):e1000041.

23. Koshy PJ, Henderson N, Logan C, et al. Interleukin 17 induces cartilage collagen breakdown: novel synergistic effects in combination with proinflammatory cytokines. Ann Rheum Dis. 2002;61(8):704-13.

24. Mease P. Psoriatic arthritis and spondyloarthritis assessment and management update. Curr Opin Rheumatol. 2013;25(3):287-96.

25. Coates LC, Fransen J, Helliwell PS. Defining minimal disease activity in psoriatic arthritis: a proposed objective target for treatment. Ann Rheum Dis. 2010;69(1):48-53.

26. Healy PJ, Helliwell PS. Measuring clinical enthesitis in psoriatic arthritis: assessment of existing measures and development of an instrument specific to psoriatic arthritis. Arthritis Care Res. 2008;59(5):686-91.

27. Bruce B, Fries JF. The Stanford Health Assessment Questionnaire: a review of its history, issues, progress, and documentation. J Rheumatol. 2003;30(1):167-78.

28. The Health Assessment Questionnaire (HAQ) and the improved HAQ (formerly called the PROMIS HAQ) (revised June 2009). Stanford: Stanford University School of Medicine, Division of Immunology & Rheumatology. 2009. Available from: http://aramis.stanford.edu/downloads/HAQ%20Instructions%20(ARAMIS)%206-30-09.pdf. Accessed on: 15 July 2015.

29. Maksymowych WP, Mallon C, Morrow S, et al. Development and validation of the Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index. Ann Rheum Dis. 2009;68(6):948-53.

30. Helliwell PS, Firth J, Ibrahim GH, et al. Development of an assessment tool for dactylitis in patients with psoriatic arthritis. J Rheumatol. 2005;32(9):1745-50.

31. Cassell SE, Bieber JD, Rich P, et al. The modified nail psoriasis severity index: validation of an instrument to assess psoriatic nail involvement in patients with psoriatic arthritis. J Rheumatol. 2007;34(1):123-9.

32. Langley RGB, Feldman SR, Nyirady J, et al. The 5-point Investigator's Global Assessment (IGA) scale: a modified tool for evaluating plaque psoriasis severity in clinical trials. J Dermatol Treat. 2015;26(1):23-31.

33. Garrett S, Jenkinson T, Kennedy LG, et al. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol. 1994;21(12):2286-91.

34. Cella D, Yount S, Sorensen M, et al. Validation of the Functional Assessment of Chronic Illness Therapy Fatigue Scale relative to other instrumentation in patients with rheumatoid arthritis. J Rheumatol. 2005;32(5);811-9.

35. van Gestel AM, Prevoo ML, van 't Hof MA, et al. Development and validation of the European League Against Rheumatism response criteria for rheumatoid arthritis. Comparison with the preliminary American College of Rheumatology and the World Health Organization/International League Against Rheumatism Criteria. Arthritis Rheum. 1996;39(1):34-40.

15.2 Unpublished References

36. Investigator's Brochure BI 655066, Psoriasis, Crohn's Disease, Ankylosing Spondylitis, 1311.P1/1311.P2/1311.P3. (c02161217)

37. Dorleacq N, Steimle-Goerttler C, Bai X, et al. Safety, tolerability, efficacy, pharmacokinetics, and pharmacodynamics of single rising i.v. (Stage 1) and s.c. (Stage 2) doses of BI 655066 in male and female patients with moderate to severe psoriasis (randomised, double-blind, placebo-controlled within dose groups) (Trial 1311.1). 26 Mar 2015. (c02434648)

38. Summary report of interim analysis at Week 48 (Trial 1311.2). 05 May 2015. (c03272682)

Appendix A. Responsibilities of the Clinical Investigator

Clinical research studies sponsored by AbbVie are subject to the Good Clinical Practices (GCP) and local regulations and guidelines governing the study at the site location. In signing the Investigator Agreement in Section 14.0 of this protocol, the investigator is agreeing to the following:

1. Conducting the study in accordance with the relevant, current protocol, making changes in a protocol only after notifying AbbVie, except when necessary to protect the safety, rights or welfare of subjects.
2. Personally conducting or supervising the described investigation(s).
3. Informing all subjects, or persons used as controls, that the drugs are being used for investigational purposes and complying with the requirements relating to informed consent and ethics committees (e.g., independent ethics committee [IEC] or institutional review board [IRB]) review and approval of the protocol and amendments.
4. Reporting adverse experiences that occur in the course of the investigation(s) to AbbVie and the site director.
5. Reading the information in the Investigator's Brochure/safety material provided, including the instructions for use and the potential risks and side effects of the investigational product(s).
6. Informing all associates, colleagues, and employees assisting in the conduct of the study about their obligations in meeting the above commitments.
7. Maintaining adequate and accurate records of the conduct of the study, making those records available for inspection by representatives of AbbVie and/or the appropriate regulatory agency, and retaining all study-related documents until notification from AbbVie.
8. Maintaining records demonstrating that an ethics committee reviewed and approved the initial clinical investigation and all amendments.

9. Reporting promptly, all changes in the research activity and all unanticipated problems involving risks to human subjects or others, to the appropriate individuals (e.g., coordinating investigator, institution director) and/or directly to the ethics committees and AbbVie.

10. Following the protocol and not make any changes in the research without ethics committee approval, except where necessary to eliminate apparent immediate hazards to human subjects.

Appendix B. List of Protocol Signatories

Name	Title	Functional Area
[redacted]	[redacted]	Clinical
		Clinical
		Statistics
		Pharmacokinetics
		Clinical
		Medical Writing

Appendix C. Study Activities

	Treatment					Follow-Up		
	V1	V2	V3	V4	V5 (EOT/Early EOT[s])	V6	EOS (EOT/Early EOT + 16 Weeks)	Follow-up Phone Call
Week	**0[a]**	**4[t]**	**12**	**24**	**36**	**48**	**52**	**56**
Day	**1**	**29 ± 4**	**85 ± 4**	**169 ± 4**	**253 ± 4**	**336 ± 4**	**365 ± 4**	**392 ± 4**
Informed Consent[b]	X							
Inclusion/exclusion criteria	X							
Medical/Surgical History[c]	X[a]							
Patient's Global Assessment of Disease Activity (VAS) (PtGA)[d]	X[a]	X	X	X	X	X	X	
Patient's Assessment of PsA Pain Intensity (VAS)[d]	X[a]	X	X	X	X	X	X	
HAQ-DI[d]	X[a]	X	X	X	X	X	X	
BASDAI[d,m]	X[a]			X	X	X	X	
SF-36v2[d]	X[a]	X	X	X	X	X	X	
FACIT-F[d]	X[a]			X	X	X		
Vital Signs[e]	X[a]	X	X	X	X	X	X	
ECG[e]	X[a]			X		X	X	
Physical Exam[e] (c = complete, t = targeted)	X-c[a]	X-t	X-t	X-t	X-t	X-t	X-c	
Concomitant Therapy[f]	X[a]	X	X	X	X	X	X	X

	Treatment					Follow-Up		
	V1	**V2**	**V3**	**V4**	**V5 (EOT/Early EOT[$])**	**V6**	**EOS (EOT/Early EOT + 16 Weeks)**	**Follow-up Phone Call**
Week	**0[a]**	**4[t]**	**12**	**24**	**36**	**48**	**52**	**56**
Day	**1**	**29 ± 4**	**85 ± 4**	**169 ± 4**	**253 ± 4**	**336 ± 4**	**365 ± 4**	**392 ± 4**
Adverse Event Assessment[g]	X[a]	X	X	X	X	X	X	X
Tender Joint Count (TJC 68)[h]	X[a]	X	X	X	X	X	X	
Swollen Joint Count (SJC 66)[h]	X[a]	X	X	X	X	X	X	
PASI[h,u]	X[a]	X	X	X	X	X	X	
BSA[h]	X[a]	X	X	X	X	X	X	
Static Physician's Global Assessment for Psoriasis (sPGA)[h,u]	X[a]	X	X	X	X	X	X	
Physician's Global Assessment of Disease Activity (PhGA) (VAS)[h]	X[a]	X	X	X	X	X	X	
Leeds Dactylitis Index (LDI)[h]	X[a]		X	X	X	X	X	
Leeds Enthesitis Index (LEI)[h]	X[a]		X	X	X	X	X	
SPARCC[h]	X[a]		X	X	X	X	X	
mNAPSI[h]	X[a]		X	X	X	X	X	
mTSS (X-ray)[i]				X		X		
Pregnancy Test[j]	X[a]	X	X	X	X	X	X	
Safety Labs (Chemistry, Hematology, Urinalysis)[k,v]	X[a]	X	X	X	X	X	X	

	Treatment					Follow-Up		
	V1	**V2**	**V3**	**V4**	**V5 (EOT/Early EOT[s])**	**V6**	**EOS (EOT/Early EOT + 16 Weeks)**	**Follow-up Phone Call**
Week	**0[a]**	**4[t]**	**12**	**24**	**36**	**48**	**52**	**56**
Day	**1**	**29 ± 4**	**85 ± 4**	**169 ± 4**	**253 ± 4**	**336 ± 4**	**365 ± 4**	**392 ± 4**
hsCRP for DAS[k]	X[a]	X	X	X	X	X	X	
Blood Sample for PK[k,l]	X[a]	X	X	X	X	X	X	
Blood Sample for ADA Assay[k,l]	X[a]	X	X	X	X	X	X	
TB screening[k,n]				X			X[r]	
Local tolerability[o]	X	X	X	X	X			
Study drug administration	X	X[p] (additional)	X	X	X			
Monitoring for hypersensitivity reaction[q]	X	X	X	X	X			
Conclusion of Subject participation								X

a. For subjects rolling over from Study 1311.5 to the OLE (Study M16-244) with ≤ 4 day delay, these procedures do not need to be repeated. Results assessed at the Week 24 visit of Study 1311.5 will serve as V1 (Week 0) visit results for Study M16-244. Subjects initiating the OLE with a delay of > 4 days and ≤ 8 weeks from completion of Study 1311.5 Week 24 visit will need to complete all activities for V1. If a subject enrolls into the OLE (Study M16-244), participation in Study 1311.5 is completed and the early completion of the Study 1311.5 is documented (EOS). All procedures of Study 1311.5 trial at Week 24 should be completed prior to the start of the Study M16-244 trial.

b. To be completed prior to initiation of Study M16-244 procedures.

c. Transcribe medical history from Study 1311.5 and record any updates.

d. Subject to complete PROs in the order listed, before any other visit assessments or treatments and, if possible, before any interaction with the investigator or other members of the study team.

e. A symptom directed physical exam should be performed when necessary and if needed for physician assessments/questionnaires. Complete physical examination will include vital sign assessment and general appearance as well as evaluation of all organ systems. Targeted physical examination will include vital sign assessment and evaluation of organ systems associated with AE(s) symptoms or laboratory abnormalities. Clinically relevant abnormal findings will be reported as baseline conditions or AEs.

f. For subjects rolling over from Study 1311.5 to the OLE without any delay, concomitant medication ending prior to first dose in Study M16-244 will be recorded in preceding Study 1311.5. Medications ongoing from preceding Study 1311.5 after first dose in Study M16-244 will be recorded in Study M16-244.

g. For subjects rolling over from Study 1311.5 to the OLE Adverse Events ending prior to completion of Study M16-244 ICF will be recorded in preceding Study 1311.5. Adverse events occurring after completing Study M16-244 ICF will be recorded in the eCRFs of Study M16-244.

h. Complete clinical assessment prior to lab sample collection and study drug administration.

i. Subjects who prematurely discontinue from the trial will not be required to collect x-rays at each designated time point, unless they received a dose within the 16 weeks prior to the scheduled time point.

j. Urine pregnancy testing will be done locally and prior to administration of study drug at all dosing visits and at each follow-up visit. Any subject with a positive urine pregnancy test must have a negative serum test performed at the central laboratory prior to enrollment or continuation in the study.

k. Complete lab sample collection after PRO, clinical assessments and before study drug administration.

l. In the event of a suspected hypersensitivity reaction or other systemic post-dose reaction, a PK/ADA and urine samples will be collected once within 24 hours of the reaction.

m. For subjects that presented with inflammatory spondylitis at baseline to Study 1311.5 based on investigator judgment.

n. QuantiFERON® TB test or PPD (purified protein derivative) skin test will be performed according to local labelling for comparator products. If the result is positive, subjects may continue in the study if further work up (according to local practice/guidelines) establishes conclusively that the subject has no evidence of active tuberculosis. If presence of latent tuberculosis is established, then tuberculosis treatment may be deferred until completion of the trial according to clinical judgment of investigator and local country guidelines and it is also necessary to report it as an adverse event in the source documents and eCRFs. If the subject is diagnosed with active tuberculosis, the subject should not receive any further study drug and follow the premature treatment discontinuation procedure (Early EOT visit) in Section 5.4.1.

o. Local tolerability at the administration site of the previous subcutaneous injection will be assessed by the investigator according to "swelling," "induration," "heat," "redness," "pain," or "other findings." Any abnormal findings at the injection site during the current visit will be reported as AEs.

p. The additional dose is given in the event that the subject has not achieved a protocol defined response (defined as an improvement in tender and swollen joint count of ≥ 20% compared with the baseline in Study 1311.5) and the investigator believes this may be beneficial to the subject.

q. Subjects should be closely monitored for signs and symptoms of hypersensitivity reactions for approximately 2 hours following the first administration, and for approximately 1 hour following subsequent doses, of study drug. Hypersensitivity reactions should be treated according to medical standards.

r. Required at EOS visit only for subjects that prematurely discontinue prior to Week 24 visit.

s. For subjects that prematurely discontinue, study drug will not be given at the early EOT visit.

t. At Week 4 visit, if the additional dose is not administered all other referenced procedures will be completed during this visit.

u. PASI and sPGA are assessed in patients with ≥ 3% BSA of psoriatic plaques at baseline in Study 1311.5 and/or current visit.

v. Subject to attend study visits in a fasted state (8 hours no food and only water). If a patient comes in non-fasted where a fasting condition is required, the visit should be performed, and the non-fasted condition documented on the laboratory requisition.

See Appendix D for Japan specific requirements.

Appendix D. Local Requirements

Local Requirements – Japan

Section 5.3.1.1: Study Procedures

Clinical Laboratory Tests

eGFR (estimated by CKD-EPI Japan formula)

Tuberculosis Screening

All subjects will be tested for TB by either the QuantiFERON-TB Gold Test (or equivalent) or a TB Skin Test or equivalent most commonly the Purified Protein Derivative (PPD) at the Week 24. If premature discontinuation occurs prior to Week 24 visit TB testing should occur at EOS visit as specified in Appendix C.

A TB Skin Test or equivalent should be utilized only when a QuantiFERON®-TB Gold Test is not possible for any reason (unless both tests are required per local guidelines).

- QuantiFERON®-TB Gold Test will be analyzed by the central laboratory (QuantiFERON test is preferred over TB Skin Test).
- If the QuantiFERON®-TB Gold Test is NOT possible (or if both the QuantiFERON®-TB Gold Test and the PPD Skin Test are required per local guidelines) the PPD Skin Test will be performed according to standard clinical practice.
- The PPD Skin Test should be read by a licensed healthcare professional between 48 and 72 hours after administration. A subject who does not return within 72 hours will need to be rescheduled for another skin test.
- The reaction will be measured in millimeters (mm) of induration and induration ≥ 5 mm is considered a positive reaction. The absence of induration will be recorded as "0 mm" not "negative."
- If PPD and/or the QuantiFERON®-TB Gold test (or IGRA equivalent) is positive, or if there is a repeat indeterminate QuantiFERON®-TB Gold test (or IGRA equivalent) upon retesting, subjects may continue in the study if further

work up (according to local practice/guidelines) establishes conclusively that the subject has no evidence of active tuberculosis.

- If the subject is diagnosed with active tuberculosis, the subject should not receive any further study drug and follow the premature treatment discontinuation procedure (Early EOT visit) in Section 5.4.1.
- **If presence of latent tuberculosis is established treatment should be initiated and maintained according to local country guidelines.** It is also necessary to report it as an adverse event in the source documents and eCRFs.
- If subject is known to have a positive QuantiFERON®-TB Gold or PPD test in Study 1311.5 Screening period do not repeat in this study.
- Subjects who have had an ulcerating reaction to the TB Skin Test in the past should not be re-exposed and should not be tested by a PPD skin test.

In the case of a tuberculosis-related adverse event, a supplemental case report form that provides additional information is be completed by the investigator or designee.

Section 7.0: Protocol Deviations

AbbVie does not allow intentional/prospective deviations from this protocol unless when necessary to eliminate an immediate hazard to study subjects. The principal investigator is responsible for complying with all protocol requirements, and applicable global and local laws regarding protocol deviations. If a protocol deviation occurs (or is identified) after a subject has been enrolled, the principal investigator is responsible for notifying Independent Ethics Committee (IEC)/Independent Review Board (IRB) regulatory authorities (as applicable), and the following AbbVie Clinical Monitor(s):

Primary Contact: Alternate Contact:

Such contact must be made as soon as possible to permit a review by AbbVie to determine the impact of the deviation on the subject and/or the study.

In Japan, the Investigator will record all protocol deviations in the appropriate medical records at site.

Section 9.3.1 Informed Consent Form and Explanatory Material

Prior to the performance of any study specific procedures, including discontinuation of any protocol prohibited medications, the investigator or representative will explain the nature of study procedures and the study to the subject and if applicable per local requirements the subject's legal representative, and all questions regarding the study will be answered. The informed consent form will be reviewed and consent to participate documented by dated signature of the representative and the person administering the informed consent.

In Japan, the principal investigator will prepare the consent form and explanatory material required to obtain subject's consent to participate in the study with the cooperation of the sponsor and will revise these documents as required. The prepared or revised consent forms and explanatory material will be submitted to the sponsor. Approval of the IRB will be obtained prior to use in the study.

Section 9.3.2: Revision of the Consent Form and Explanatory Material

In Japan, when important new information related to the subject's consent becomes available, the principal investigator will revise the consent form and explanatory material based on the information without delay and will obtain the approval of the IRB prior to use in the study. The investigator will provide the information, without delay, to each subject already participating in the study, and will confirm the intention of each subject to continue the study or not. The investigator shall also provide a further explanation using the revised form and explanatory material and shall obtain written consent from each subject of their own free will to continue participating in the study.

Section 13.0: Completion of the Study

The investigator will conduct the study in compliance with this protocol and complete the study within the timeframe specified in the contract between the investigator **(Director of the Site in Japan)** and AbbVie. Continuation of this study beyond this date must be mutually agreed upon in writing by both the investigator **(Director of the Site in Japan)** and AbbVie. The investigator will provide a final report to the IEC/IRB following conclusion of the study, and will forward a copy of this report to AbbVie or their representative.

The investigator **(Director of the Site in Japan)** must retain any records related to the study according to local requirements. If the investigator **(Director of the Site in Japan)** is not able to retain the records, he/she must notify AbbVie to arrange alternative archiving options.

AbbVie will select the signatory investigator from the investigators who participate in the study. Selection criteria for this investigator will include level of participation as well as significant knowledge of the clinical research, investigational drug and study this protocol. The signatory investigator for the study will review and sign the final study report in accordance with the European Agency for the Evaluation of Medicinal Products (EMEA) Guidance on Investigator's Signature for Study Reports.

The end-of-study is defined as the date of the last subject's last visit.

Appendix C: Study Activities Table

	Treatment					Follow-Up		
	V1	**V2**	**V3**	**V4**	**V5 (EOT/Early EOT)**	**V6**	**EOS (EOT/Early EOT + 16 Weeks)**	**Follow-up Phone Call**
Week	**0**	**4**	**12**	**24**	**36**	**48**	**52**	**56**
Day	**1 ± 4**	**29 ± 4**	**85 ± 4**	**169 ± 4**	**253 ± 4**	**336 ± 4**	**365 ± 4**	**365 ± 4**
HBV DNA*	X			X			X	

* If subject had positive Hepatitis B Core Antibody or Hepatitis B Surface Antibody in Study 1311.5 and the reflex Hepatitis B virus DNA quantification level was undetectable at screening the HBV DNA level must be monitored at least every 6 months.

In the case of a tuberculosis-related adverse event, a supplemental case report form that provides additional information is be completed by the investigator or designee.

Local Requirements – Germany

Section 5.3.1.1 Study Procedures – X-Ray Assessments

The modified Total Sharp Score (mTSS) method, including distal interphalangeal joints, will be used to evaluate radiographic evidence of damage.[19] X-rays of hands, wrists and feet. The x-rays will be performed at two time points (Weeks 24 and 48, detailed in Appendix C). Images will be read centrally for each subject in a random order and without knowledge of time point or subject identity. Subjects who prematurely discontinue from study drug will not be required to collect x-rays at each designated time point, unless they received a dose within the 16 weeks prior to the scheduled time point.

For subjects who have had an X-Ray performed within 2 weeks before the scheduled protocol X-ray assessment, no additional X-Rays should be performed.

Local Requirements – France

Section 5.2.1 Inclusion Criterion 2

Women of childbearing potential must agree to use at least one of the following methods of contraception throughout the study including **20 weeks** after the last study drug dose is given:

- combined (estrogen and progestogen containing) hormonal birth control (oral, intravaginal, transdermal) associated with inhibition of ovulation initiated at least one month prior to study participation
- progestogen-only hormonal birth control (oral, injectable, implantable) associated with inhibition of ovulation initiated at least one month prior to study participation
- bilateral tubal occlusion/ligation
- intrauterine device (IUD)
- intrauterine hormone-releasing system (IUS)
- Vasectomized sexual partner(s) (the vasectomized partner should have received medical assessment of the surgical success and is the sole sexual partner of the trial participant).
- True abstinence: Refraining from heterosexual intercourse when this is in line with the preferred and usual lifestyle of the subject (periodic abstinence [e.g., calendar, ovulation, symptothermal, post-ovulation methods] and withdrawal are not acceptable).

Women of childbearing potential are defined as having experienced menarche and are:

- not postmenopausal (12 months with no menses without an alternative medical cause)
- not permanently sterilized (e.g., hysterectomy, bilateral oophorectomy or bilateral salpingectomy).

Section 5.2.2 Exclusion Criterion 1

1. Female subject who is pregnant, breastfeeding or is considering becoming pregnant during study participation, including **20 weeks** after the last dose of study drug is given.

Section 5.2.4 – Contraception Recommendations and Pregnancy

Female subjects of childbearing potential must be ready and able to use highly effective methods of birth control per ICH M3(R2) that result in a low failure rate of less than 1% per year when used consistently and correctly. Or subjects must have only vasectomized sexual partner(s), or be abstinent. The method chosen must be practiced throughout the study including **20 weeks** after the last dose of study drug is given.

Women of childbearing potential are defined as having experienced menarche and are:

- not postmenopausal (12 months with no menses without an alternative medical cause)
- not permanently sterilized (e.g., tubal occlusion, hysterectomy, bilateral oophorectomy or bilateral salpingectomy).

The following is a list of accepted contraception methods:

- combined (estrogen and progestogen containing) hormonal birth control (oral, intravaginal, transdermal) associated with inhibition of ovulation initiated at least 1 month prior to study participation
- progestogen-only hormonal birth control associated with inhibition of ovulation initiated at least one month prior to study participation
- bilateral tubal occlusion/ligation
- intrauterine device (IUD)
- intrauterine hormone-releasing system (IUS)

- Vasectomized sexual partner(s) (the vasectomized partner should have received medical assessment of the surgical success and is the sole sexual partner of the trial participant).
- True abstinence: Refraining from heterosexual intercourse when this is in line with the preferred and usual lifestyle of the subject (periodic abstinence [e.g., calendar, ovulation, symptothermal, post-ovulation methods] and withdrawal are not acceptable).

In addition, both female subjects of childbearing potential and male subjects with female partners of childbearing potential, taking MTX as background medication, must follow the national regulatory guidelines regarding contraception while taking these medications.

See Pregnancy Testing paragraph in Section 5.3.1.1 for pregnancy testing instructions.

Appendix E. Joint Assessment

Joint counts will be performed by assessor(s) who must be well trained and part of the site personnel. Whenever possible, the same evaluator should perform these assessments at all visits.

Number of Tender Joints:

The 68 joints assessed for tenderness include the 2 temporomandibular, 2 sternoclavicular, 2 acromioclavicular joints, 2 shoulders, 2 elbows, 2 wrists, 10 metacarpophalangeal, 10 proximal interphalangeal, 8 distal interphalangeal joints of the hands, the 2 hips, 2 knees, 2 ankles 2 mid-tarsal, 10 metatarsophalangeal, and 10 proximal interphalangeal joints of the feet.

Joints are to be scored as either tender (1) or not tender (0), replaced (9) or not assessed (99).

Number of Swollen Joints:

The 66 joints to be examined for swelling are the same as those examined for tenderness, however excluding both hip joints.

Joints are to be scored as either swollen (1) or not swollen (0), replaced (9) or not assessed (99).

Synovial fluid and/or soft tissue swelling but not bony overgrowth represents a positive result for swollen joint count.

Data will be recorded for tender and swollen joints (right or left side), i.e., a box (no, yes or not applicable) needs to be ticked for all joints. The total number of tender and swollen joints (right and left) will be automatically calculated in the eCRF.

Joint	Left		Right	
	Tender	**Swollen**	**Tender**	**Swollen**
Temporomandibular				
Acromioclavicular				
Sternoclavicular				
Shoulder#				
Elbow#				
Wrist#				
MCP1#				
MCP2#				
MCP3#				
MCP4#				
MCP5#				
IP of the thumb#				
PIP of fingers 2#				
PIP of fingers 3#				
PIP of fingers 4#				
PIP of fingers 5#				
DIP of fingers 2				
DIP of fingers 3				
DIP of fingers 4				
DIP of fingers 5				
Hip*				
Knee#				
Ankle				
Mid-Tarsal				
MTP1				
MTP2				
MTP3				
MTP4				
MTP5				
IP of great toe				
PIP of toes 2				

Joint	Left		Right	
	Tender	**Swollen**	**Tender**	**Swollen**
PIP of toes 3				
PIP of toes 4				
PIP of toes 5				

* Hip will only be assessed for TJC (Tender Joint Counts), not for SJC (Swollen Joint Count).

Joints which will also count for DAS28-hsCRP evaluation.

Appendix F. PASI SCORE Definitions and Use

The PASI score is an established measure of clinical efficacy for psoriasis medications.[3]

The PASI is a tool which provides a numeric scoring for patients overall psoriasis disease state, ranging from 0 to 72. It is a linear combination of percent of surface area of skin that is affected and the severity of erythema, infiltration, and desquamation over four body regions.

The endpoints used are based on the percent reduction from baseline, generally summarized as a dichotomous outcome based on achieving over an X% reduction (or PASIX), where X is 50, 75, 90 and 100.

To calculate the PASI score, the four main body areas are assessed: **head (h), trunk (t), upper extremities (u) and lower extremities (l)**. These correspond to 10, 30, 20 and 40% of the total body area respectively.

The **area of psoriatic involvement** of these four areas (Ah, At, Au, and Al) is given a numerical value: 0 = no involvement, 1 = < 10%, 2 = 10 to < 30%, 3 = 30 to < 50%, 4 = 50 to < 70%, 5 = 70 to < 90%, and 6 = 90 to 100% involvement.

The **signs of severity, erythema (E), infiltration (I) and desquamation (D)** of lesions are assessed using a numeric scale 0 – 4 where 0 is a complete lack of cutaneous involvement and 4 is the severest possible involvement; scores are made independently for each of the areas, h, t, u and l and represents a composite score for each area. An illustration of judging erythema follows: 0 = no erythema, 1 = slight erythema, 2 = moderate erythema, 3 = striking erythema, and 4 = exceptionally striking erythema.

The PASI score is calculated according to the following formula:

PASI = 0.1(Eh+Ih+Dh)Ah + 0.3(Et+It+Dt)At + 0.2(Eu+Iu+Du)Au + 0.4(El+Il+Dl)Al

Appendix G. Static Physician Global Assessment (sPGA)

This 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 (Table 3).[32]

The assessment is considered "static" which refers to the patients disease state at the time of the assessments, without comparison to any of the patient's previous disease states, whether at Baseline or at a previous visit.

A lower score indicates less body coverage, with 0 being clear and 1 being almost clear.

The investigator (or qualified site personnel) scores the erythema, induration and scaling of all psoriatic lesions from 0 – 4 based on the following descriptors:

Erythema

0	Normal (post-inflammatory hyper/hypopigmentation may be present)
1	Faint, diffuse pink or slight red coloration
2	Mild (light red coloration)
3	Definite red coloration (Dull to bright red)
4	Bright to Deep red coloration of lesions

Induration (Plaque Elevation)

0	None
1	Just detectable (possible slight elevation above normal skin)
2	Mild thickening (slight but definite elevation, typically edges are indistinct or sloped)
3	Clearly distinguishable to moderate thickening (marked definite elevation with rough or sloped edges)
4	Severe thickening with hard edges (marked elevation typically with hard or sharp edges)

Scaling

0	No scaling
1	Minimal focal scaling (surface dryness with some desquamation)
2	Predominately fine scaling (fine scale partially or mostly covering lesions)
3	Moderate scaling (coarser scale covering most or all of the lesions)
4	Severe/coarse scaling covering almost all or all lesions (coarse, non-tenacious scale predominates)

Scoring

A composite score is generated from the above data and the final sPGA is determined from this composite 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

Table 3. sPGA Rating Scale for Overall Psoriatic Disease

Score	Short Description	Detailed Description
0	clear	No signs of psoriasis. Post-inflammatory hyperpigmentation may be present.
1	almost clear	Normal to pink coloration. Just detectable (possible slight elevation above normal skin). No to minimal focal scaling.
2	mild	Pink to light red coloration. Mild thickening (slight but definite elevation, typically edges are indistinct or sloped). Predominantly fine scaling.
3	moderate	Dull to bright red coloration. Clearly distinguishable to moderate thickening. Moderate scaling.
4	severe	Bright to deep dark red coloration. Severe thickening with hard edges. Severe coarse scaling covering almost all or all lesions.

Appendix H. Leeds Dactylitis Index (LDI)

The LDI basic measures the ratio of the circumference of the affected digit to the circumference of the digit on the opposite hand or foot, using a minimum difference of 10% to define a dactylitic digit.[30] The ratio of circumference is multiplied by a tenderness score, using a modification of LDI which is a binary score (1 for tender, 0 for non-tender). If both sides are considered involved, or the circumference of the contralateral digit cannot be obtained, the number will be compared to data provided in the standard reference tables (Table 4 and Table 5). This modification is referred to as LDI basic and will be applied in this study. The LDI requires a finger circumference gauge or a tape measure to measure digital circumference.

Dactylitis Count

The dactylitis count is the number of fingers and toes with dactylitis, with a range of 0 – 20.

Presence of Dactylitis

If dactylitis is present with any finger or toe, the subject is counted as a subject with dactylitis.

Table 4. Hands (in cm)

Digit	Men	Women
Thumb	7.0	5.8
Index	6.3	5.4
Middle	6.3	5.4
Ring	5.9	5.0
Little	5.2	4.4

Table 5. Feet (in cm)

Digit	Men	Women
Central toe	8.2	7.2
Second	5.2	4.6
Middle	5.0	4.4
Fourth	5.0	4.4
Little	5.2	4.5

Appendix I. Leeds Enthesitis Index (LEI)

LEI is a validated enthesitis index that uses 6 sites for evaluation of enthesitis: lateral epicondyle humerus left and right, Achilles tendon insertion left and right and medial condyle femur left and right. The LEI demonstrated substantial to excellent agreement with other scores in the indication of psoriatic arthritis.[26]

Enthesitis Count

Tenderness on examination is recorded as either present (1) or absent (0) for each of the 6 sites, for an overall score range of 0 – 6.

Presence of Enthesitis

If enthesitis is present with any of the 6 sites (lateral epicondyle humerus left and right, Achilles tendon insertion left and right and medial condyle femur left and right), the subject is counted as a subject with enthesitis.

Appendix J. Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index

Enthesial sites examined include medial epicondyle (left and right), lateral epicondyle (left and right), supraspinatus insertion into greater tuberosity of humerus (left and right), greater trochanter (left and right), quadriceps insertion into superior border of patella (left and right), patellar ligament insertion into inferior pole of patella or tibial tubercle (left and right), Achilles tendon insertion into calcaneum (left and right), plantar fascia insertion into calcaneum (left and right).[29]

Enthesitis Count

Tenderness on examination is recorded as either present (1) or absent (0) for each of the 16 sites, for an overall score range of 0 – 16.

Appendix K. mNAPSI – Modified Nail Psoriasis Severity Index

Modified NAPSI Instructions[31]

This tool will ask you to assess each abnormality for each of a subject's fingernails. If you question which grade to give, your answer should be the lower of the grades.
Three features or groups of features (pitting, onycholysis and oil-drop dyschromia, and crumbling) of each fingernail will be graded on a scale from 0 to 3, according to the directions below. Four features (leukonychia, splinter hemorrhages, hyperkeratosis, and red spots in the lunula) will be graded as either present or absent for each fingernail.
After you have viewed all the fingernails of a subject, consider all aspects of all of the subject's fingernails and place a mark on the visual analog scale giving a global assessment of their fingernails.

1. **Onycholysis:** Separation of the nail plate from the nail bed. The separated part of the nail is opaque and can have white, yellow, or greenish tinge. If there is a piece of nail missing, estimate where the nail normally would have ended at the end of the nail bed, and count that missing part as involved in onycholysis.

   Oil-drop (salmon patch) dyschromia: Reddish-brown discoloration under the nail plate.

   Onycholysis and oil-drop dyschromia are considered together. When looking at the nail, combine the total percentage area of the nail that is affected by either and use that combined total to score the nail.

Score	Percent of Nail with Onycholysis or Oil-Drop Dyschromia Present
0	No onycholysis or oil drop dyschromia present
1	1 – 10% of the nail has onycholysis or oil-drop dyschromia
2	11 – 30% of the nail has onycholysis or oil-drop dyschromia
3	> 30% of the nail has onycholysis or oil-drop dyschromia

2. **Pitting:** Small, sharply defined depressions in the nail surface. Pits are discrete abnormalities ("ice-pick-like"). If there is nail plate crumbling that is confluent

with pits, do not score for pits. If the pits are separate from crumbling, they may be scored regardless of whether crumbling is present or not.

Score	Number of Pits
0	0
1	1 – 10
2	11 – 49
3	> 50

3. **Nail plate crumbling:** Crumbling or fragmentation of friable nail plate which may be associated with confluent pitting. Crumbling involves alteration of the nail plate surface. Horizontal ridging of the nail, "wave-like" appearance, and horizontal lines are all features of crumbling.

Score	Percent of Nail with Crumbling Present
0	No crumbling
1	1 – 25% of the nail has crumbling
2	26 – 50% of the nail has crumbling
3	> 50% of the nail has crumbling

The next 4 abnormalities are scored only by their presence or absence. A score of 1 indicates present and a score of zero indicates not present.

1. **Leukonychia:** White spots in the nail plate due to psoriasis in the mid matrix. Leukonychia are just color changes. If it appears that there is depression or irregularity to the nail surface, this may be pitting or crumbling, not leukonychia. If the leukonychia is adjacent to, or confluent with crumbling or pits, it is counted as part of the crumbling or pitting and not as a separate abnormality.
2. **Splinter hemorrhages:** Small, longitudinal, linear, dark brown hemorrhage under the fingernail.
3. **Nail bed hyperkeratosis:** Thickened keratin in the nail bed.

4. **Red spots in the lunula:** Small pink or red macules in the lunula.

Appendix L. ACR Response Criteria

ACR response criteria is scored as follows:[2]

ACR 20:

- At least 20% improvement in SJC* compared to baseline **AND**
- At least 20% improvement in TJC* compared to baseline **AND**
- At least 20% improvement in at least 3 out of the following 5 variables

ACR 50:

- At least 50% improvement in SJC* compared to baseline **AND**
- At least 50% improvement in TJC* compared to baseline **AND**
- At least 50% improvement in at least 3 out of the following 5 variables

ACR 70:

- At least 70% improvement in SJC* compared to baseline **AND**
- At least 70% improvement in TJC* compared to baseline **AND**
- At least 70% improvement in at least 3 out of the following 5 variables

1. Patient's Assessment of PsA Pain Intensity (VAS) (See Appendix R)
2. Patient's Global Assessment of Disease (VAS) (See Appendix R)
3. Physician's Global Assessment of Disease Activity (VAS) (See Appendix M)
4. Patient's Assessment of Disability on HAQ (See Appendix R)
5. Acute phase reactant (serum CRP) (serum hs-CRP)

* SJC and TJC are evaluated according to the complete joint count (see Appendix E).

Appendix M. Physician's Global Assessment of Disease Activity (PhGA)

The physician's global assessment of disease activity will be performed using 100 mm VAS ranging from no disease activity to maximal disease activity, after the question "Considering all the ways the disease affects your patient, draw a line on the scale for how well his or her condition is today." To enhance objectivity, the physician must not be aware of the specific patient's global assessment of disease activity, when performing his own assessment on that subject.

Appendix N. Minimal Disease Activity

The proportion of subjects achieving minimal disease activity (MDA) will be analysed. A patient is classified as achieving MDA when meeting at least 5 of the 7 following criteria are met:[25]

- Tender joint count ≤ 1
- Swollen joint count ≤ 1
- PASI ≤ 1 or BSA ≤ 3%
- Patient Assessment of Pain-VAS ≤ 15
- Patient Global Assessment of Disease Activity VAS ≤ 20
- HAQ-DI ≤ 0.5
- Tender entheseal points ≤ 1

Appendix O. DAS28 – hsCRP

DAS28-hsCRP will be calculated taking the following variables into account:[25]

- TJC (on 28 joints, see Appendix E)
- SJC (on 28 joints, see Appendix E)
- Patient's global assessment of the disease on VAS (0 – 100)
- Serum hsCRP level (mg/L)

The formula used for DAS28 - hsCRP is: $DAS28=0.56*\sqrt{(TJC)} + 0.28*\sqrt{(SJC)} + 0.36*Ln(hsCRP+1) + 0.014*VAS + 0.96$

Appendix P. EULAR Response Criteria

The EULAR response criteria can be defined using the table below:[35]

	Improvement in DAS28 from Baseline:		
DAS28 at Endpoint	**> 1.2**	**> 0.6 and ≤ 1.2**	**≤ 0.6**
≤ 3.2	Good		
> 3.2 and ≤ 5.1		Moderate	
> 5.1			None

Appendix Q. PsARC Response

A subject is defined as a PsARC responder if, and only if, they have an improvement in two of the following four factors (with at least one factor being a joint count) and no worsening in the remaining factors:[6]

- Patient global assessment of disease activity (0 – 100 mm VAS scale, improvement defined as decrease of ≥ 20 mm)
- Physician global assessment of disease activity (0 – 100 mm VAS scale, improvement defined as decrease ≥ 20 mm)
- Tender 68-joint count (improvement defined as decrease of ≥ 30%)
- Swollen 66-joint count (improvement defined as decrease of ≥ 30%)

Appendix R. Patient Reported Outcomes

Patient's Assessment of PsA Pain Intensity

The pain-VAS will be self-administered by the patient at visits indicated in the Appendix C.

The patient's assessment of PsA pain intensity will be performed using a horizontal 100 mm visual analog scale (VAS), ranging from 0 (no pain) to 100 (severe pain) after the question:

"Please indicate with a vertical mark (|) through the horizontal line the most pain you had from your psoriatic arthritis today."

Patient's Global Assessment of Disease Activity

The patient global assessment VAS will be self-administered by the patient at visits indicated in Appendix C.

The patient's global assessment of disease activity will be performed using a horizontal 100 mm VAS, ranging from 0 (very well) to 100 (very poor) after the question:

"Considering all the ways psoriatic arthritis affects you, please indicate with a vertical mark (|) through the horizontal line how well you are doing today."

Health Assessment Questionnaire Disability Index (HAQ-DI)

The HAQ-DI is a twenty-item patient reported outcome instrument that assesses current physical function/disability. The HAQ-DI covers eight categories (dressing and grooming, hygiene, arising, reach, eating, grip, walking and common daily activities). There are four response options, ranging from 0 (no difficulty) to 3 (unable to do). HAQ-DI score is reported as a mean score between 0 and 3 by dividing the total score by the number of items answered.[28]

The HAQ-DI has been the most-widely used instrument to assess physical function clinical trials of treatments for rheumatoid and psoriatic arthritis and has extensive evidence of its validity and other psychometric properties in this context.[28]

The HAQ-DI will be self-administered by the patient at visits indicated in Appendix C.

Medical Outcome Short Form Health Survey (SF-36) Version 2 (Acute Form)[1,4]

The SF-36 is a widely used and extensively studied instrument to measure health-related quality of life among healthy subjects and patients with acute and chronic conditions. It consists of eight subscales that can be scored individually: Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional, and Mental Health.[4] Two overall summary scores, the Physical Component Summary (PCS) and the Mental Component Summary (MCS) also can be computed.[1] The SF-36 has proven useful in monitoring general and specific populations, comparing the relative burden of different disease, differentiating the health benefits produced by different treatments, and in screening individual subjects.

The purpose of the SF-36 in this study is to assess the Health Related Quality of Life (HRQoL) of subjects. Given the acute nature of this disease, version 2, with a 1-week recall period, will be used in this study.

Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F)[7,8,34]

The FACIT-F is a 13-item questionnaire that assesses self-reported fatigue and its impact upon daily activities and function.

The purpose of FACIT-F in this study is to assess the impact of fatigue on subjects with PsA.

Number of items: 13 items.

Response options/scale: Answers are based on a 5-point Likert scale. Responses of "not at all," "a little," "somewhat," "quite a bit," and "very much" are available for each question, and correspond to scores of 0, 1, 2, 3, and 4, respectively.

Recall period for items: 7 days.

BASDAI (Bath Ankylosing Spondylitis Disease Activity Index)[33]

Each question is answered on a 0 to 10 scale. For Questions 1 – 5, 0 means none and 10 means very severe; for Question 6, 0 means 0 hours and 10 means 2 or more hours. All questions refer to last week.

1. How would you describe the overall level of fatigue/tiredness you have experienced?
2. How would you describe the overall level of AS neck, back or hip pain you have had?
3. How would you describe the overall level of pain/swelling in joints other than neck, back or hips you have had?
4. How would you describe the overall level of discomfort you have had from any areas tender to touch or pressure?
5. How would you describe the overall level of morning stiffness you have had from the time you wake up?
6. How long does your morning stiffness last from the time you wake up?

Calculation of BASDAI: compute the mean of Questions 5 and 6. Calculate the sum of the values of Questions 1 – 4 and add the result to the mean of Questions 5 and 6. Divide the result by 5.

Appendix S. Rheumatology Common Toxicity Criteria v.2.0 Example

For designation of adverse event terms not shown in the Rheumatology Common Toxicity Criteria v.2.0[11] table, the approach described in Row 1 should be used.

Rheumatology Common Toxicity Criteria v.2.0				
Standardizing Assessment and Reporting of Adverse Effects in Rheumatology Clinical Trials: Enabling Description of Comparative Safety Profiles for Antirheumatic Therapies				
	1 – Mild Asymptomatic, or transient Short duration (< 1 week) No change in life style No medication or OTC	**2 – Moderate** Symptomatic Duration (1 – 2 weeks) Alter lifestyle occasionally meds relieve. (May be prescription), Study drug continued	**3 – Severe** Prolonged symptoms, reversible, major functional impairment Prescription meds/partial relief May be hospitalized < 24 hr Temporary study drug discontinuation, or/and dose reduced	**4 – Includes Life-Threatening** At risk of death Substantial disability, especially if permanent. Multiple meds Hospitalised > 24 hr Study drug discontinued
A. Allergic/Immunologic				
A1. Allergic reaction/hypersensitivity (includes drug fever)	Transient rash: drug fever < 38°C: transient, asymptomatic bronchospasm	Generalised urticaria responsive to meds; or drug fever > 38°C, or reversible bronchospasm	Symptomatic bronchospasm requiring meds; symptomatic urticaria persisting with meds, allergy related oedema/angioedema	Anaphylaxis, laryngeal/pharyngeal oedema, requiring resuscitation
A2. Autoimmune reaction	Seriologic or other evidence of autoimmune reaction, but patient asymptomatic: all organ function normal and no treatment is required (e.g., vitiligo)	Evidence of autoimmune reaction involving a non-essential organ or functions, requiring treatment other than immunosuppressive drugs (e.g., hypothyroidism)	Reversible autoimmune reaction involving function of a major organ or toxicity requiring short term immunosuppressive treatment (e.g., transient colitis or anaemia)	Causes major organ dysfunction, or progressive, not reversible, or requires long-term administration of high-dose immunosuppressive therapy
A3. Rhinitis (includes sneezing, nasal stuffiness, post nasal discharge)	Transient, non-prescription meds relieve	Prescription med. required, slow	Corticosteroids or other prescription med. with persistent disabling symptoms such as impaired exercise tolerance	NA

A. Allergic/Immunologic (Continued)				
A4. Serum sickness	Transient, non-prescription meds relieve	Symptomatic, slow response to meds (e.g., oral corticosteroids)	Prolonged; symptoms only partially relieved by meds; parenteral corticosteroids required	Major organ dysfunction, requires long-term high-dose immunosuppressive therapy
A5. Vasculitis	Localised, not requiring treatment; or rapid response to meds; cutaneous	Symptomatic, slow response to meds (e.g., oral corticosteroids)	Generalised, parenteral corticosteroids required or/and short duration hospitalisation	Prolonged, hospitalisation, ischemic changes, amputation
B. Cardiac				
B1. Arrhythmia	Transient, asymptomatic	Transient, but symptomatic or recurrent, responds to meds	Recurrent/persistent; maintenance prescription	Unstable, hospitalisation required, parenteral meds
B2. Cardiac function decreased	Asymptomatic decline in resting ejection fraction by > 10%, but < 20% of baseline value	Asymptomatic decline of resting ejection fraction ≥ 20% of baseline value	CHF responsive to treatment	Severe or refractory CHF
B3. Edema	Asymptomatic (e.g., 1 + feet/calves), self-limited, no therapy required	Symptomatic (e.g., 2 + feet/calves), requires therapy	Symptoms limiting function (e.g., 3 + feet/calves, 2 + thighs), partial relief with treatment prolonged	Anasarca; no response to treatment
B4. Hypertension (new onset or worsening)	Asymptomatic, transient increase by > 20 mmHg (diastolic) or to > 150/100 if previously normal, no therapy required	Recurrent or persistent increase > 150/100 or by > 10 mmHg (diastolic), requiring and responding readily to treatment	Symptomatic increase > 150/100, > 20 mmHg, persistent, requiring multi agency therapy, difficult to control	Hypertensive crisis
B5. Hypotension (without underlying diagnosis)	Transient, intermittent, asymptomatic, orthostatic decrease in blood pressure > 20 mmHg	Symptomatic, without interference with function, recurrent or persistent > 20 mmHg decrease, responds to treatment	Syncope or symptomatic, interferes with function, requiring therapy and sustained medical attention, dose adjustment or drug discontinuation	Shock

B. Cardiac (Continued)				
B6. Myocardial ischaemia	Transient chest pain/ECG changes; rapid relief with nitro	Recurring chest pain, transient ECG ST-T changes; treatment relieves	Angina with infarction, no or minimal functional compromise, reduce dose or discontinue study drug	Acute myocardial infarction, arrthymia or/and CHF
B7. Pericarditis/pericardial effusion	Rub heard, asymptomatic	Detectable effusion by echocardiogram, symptomatic NSAID required	Detectable on chest x-ray, dyspnoea; or pericardiocentesis; requires corticosteroids	Pulsus alternates with low cardiac output; requires surgery
B8. Phlebitis/thrombosis/Embolism (excludes injection sites)	Asymptomatic, superficial, transient, local, or no treatment required	Symptomatic, recurrent, deep vein thrombosis, no anticoagulant therapy required	Deep vein thrombosis requiring anticoagulant therapy	Pulmonary embolism
C. General (Constitutional)				
C1. Fatigue/malaise (asthenia)	Increase over baseline; most usual daily functions maintained, short term	Limits daily function intermittently over time	Interferes with basic ADL, persistent	Unable to care for self, bed or wheelchair bound > 50% of day debilitating, hospitalisation
C2. Fever (pyrexia) (note: fever due to drug allergy should be coded as allergy)	Transient, few symptoms 37.7 – 38.5°C	Symptomatic, recurrent 38.6 – 39.9°C. Relieved by meds	≥ 40°C; ≤ 24 h, persistent symptoms; partial response to meds	≥ 40°C, debilitating, > 24 h, hospitalisation; no relief with meds
C3. Headache	Transient or intermittent, no meds or relieved with OTC	Persistent, recurring, non-narcotic analgesics relieve	Prolonged with limited response to narcotic medicine	Intractable, debilitating, requires parenteral meds
C4. Insomnia	Difficulty sleeping, short term, no interfering with function	Difficulty sleeping interfering with function, use of prescription med	Prolonged symptoms, with limited response to narcotic meds	Debilitating, hospitalisation; no relief with meds
C5. Rigors, chills	Asymptomatic, transient, no meds, or non-narcotic meds relieve	Symptomatic, narcotic meds relieve	Prolonged symptoms, with limited response to narcotic meds	Debilitating, hospitalisation; no relief with meds
C6. Sweating (diaphoresis)	Episodic, transient	Frequent, short term	Frequent, drenching, disabling	Dehydration, requiring IV fluids/hospitalization > 24 hrs

C. General (Constitutional) (Continued)				
C7. Weight gain	5% – 9.9%	10% – 19.9%	20% – 30%	NA
C8. Weight loss	5% – 9.9%	10% – 19.9%	20% – 30%	NA
D. Dermatologic				
D1. Alopecia	Subjective, transient	Objective, fully reversible	Patchy, wig used, partly reversible	Complete, or irreversible even if patchy
D2. Bullous eruption	Localised, asymptomatic	Localised, symptomatic, requiring treatment	Generalised, responsive to treatment; reversible	Prolonged, generalised, or requiring hospitalisation for treatment
D3. Dry skin	Asymptomatic, controlled with emollients	Symptoms eventually (1 – 2 wks) controlled with emollients	Generalised, interfering with ADL > 2 wks, persistent pruritis, partially responsive to treatment	Disabling for extended period, unresponsive to ancillary therapy and requiring study drug discontinuation for relief
D4. Injection site reaction	Local erythema, pain, pruritis, < few days	Erythema, pain, oedema, may include superficial phlebitis, 1 – 2 wks	Prolonged induration, superficial ulceration; includes thrombosis	Major ulceration necrosis requiring surgery
D5. Petechiae (without vasculitis)	Few, transient asymptomatic	Dependent areas, persistent up to 2 wks	Generalised, responsive to treatment; reversible	Prolonged, irreversible, disabling
D6. Photosensitivity	Transient erythema	Painful erythema and oedema requiring topical treatment	Blistering or desquamation, requires systematic corticosteroids	Generalised exfoliation or hospitalisation
D7. Pruritis	Localised, asymptomatic, transient, local treatment	Intense, or generalised, relieved by systematic medication	Intense or generalised; poorly controlled despite treatment	Disabling, irreversible
D8. Rash (not bullous)	Erythema, scattered macular/popular eruption; pruritis transient; TOC or no meds	Diffuse macular/popular eruption or erythema with pruritus; dry desquamation; treatment required	Generalised, moist desquamation, requires systemic corticosteroids; responsive to treatment; reversible	Exfoliative or ulcerating; or requires hospitalisation; or parenteral corticosteroids

D. Dermatologic (Continued)				
D9. Induration/fibrosis/Thickening (not sclerodermal)	Localized, high density on palpation, reversible, no effect on ADL and not disfiguring	Local areas < 50% body surface, not disfiguring, transient interference with ADL, reversible	Generalized, disfiguring, interferes with ADL, reversible	Disabling, irreversible, systemic symptoms
E. Ear/Nose/Throat				
E1. Hearing loss	Transient, intermittent, no interference with function	Symptomatic, treatment required, reversible	Interferes with function; incomplete response to treatment	Irreversible deafness
E2. Sense of smell	Slightly altered	Markedly altered	Complete loss, reversible	Complete loss, without recovery
E3. Stomatitis	Asymptomatic	Painful, multiple, can eat	Interferes with nutrition, slowly reversible	Requires enteral support; residual dysfunction
E4. Taste disturbance (dysgeusia)	Transiently altered; metallic	Persistently altered; limited effect on eating	Disabling, effect on nutrition	NA
E5. Tinnitus	Intermittent, transient, no interference with function	Requires treatment, reversible	Disabling, or associated with hearing loss	Irreversible deafness
E6. Voice changes (includes hoarseness, loss of voice, laryngitis)	Intermittent hoarseness, able to vocalise	Persistent hoarseness, able to vocalise	Whispered speech, slow return of ability to vocalise	Unable to vocalize for extended
E7. Xerostomia (dry mouth)	Transient dryness	Relief with meds	Interferes with nutrition, slowly reversible	Extended duration interference with nutrition, requires parenteral nutrition
F. Eye/Ophthalmologic				
F1. Cataract	Asymptomatic, no change in vision, non-progressive	Symptomatic, partial visual loss, progressive	Symptoms impairing function, vision loss requiring treatment, including surgery	NA
F2. Conjunctivitis	Asymptomatic, transient, rapid response to treatment	Symptomatic, responds to treatment, changes not interfering with function	Symptoms prolonged, partial response to treatment, interferes with function	NA

F. Eye/Ophthalmologic (Continued)				
F3. Lacrimation increased (tearing, watery eyes)	Symptoms not requiring treatment, transient	Symptomatic, treatment required, reversible	Unresponsive to treatment with major effect on function	NA
F4. Retinopathy	Asymptomatic, non-progressive, no treatment	Reversible change in vision; readily responsive to treatment	Disabling change in vision ophthalmological findings reversible, sight improves over time	Loss of sight
F5. Vision changes (e.g., blurred, photophobia, night blindness, vitreous floaters)	Asymptomatic, transient, no treatment required	Symptomatic, vision changes not interfering with function, reversible	Symptomatic, vision changes interfering with function	Loss of sight
F6. Xerophtalmia (dry eyes)	Mild scratchiness	Symptomatic without interfering with function, requires artificial tears	Interferes with vision/function, corneal ulceration	Loss of sight
G. Gastrointestinal				
G1. Anorexia	Adequate food intake, minimal weight loss	Symptoms requiring oral nutritional supplementation	Prolonged, requiring iv support	Requires hospitalization for nutritional support
G2. Constipation	Asymptomatic, transient, responds to stool softener, OTC laxatives	Symptomatic, requiring prescription laxatives, reversible	Obstipation requiring medical intervention	Bowel obstruction. Surgery required.
G3. Diarrhea	Transient, increase of 2 – 3 stools/day over pre-treatment (no blood or mucus), OTC agents relieve	Symptomatic, increase 4 – 6 stools/day, nocturnal stools, cramping, requires treatment with prescription meds	Increase > 6 stools/day, associated with disabling symptoms, e.g., incontinence, severe cramping, partial response to treatment.	Prolonged, dehydration, unresponsive to treatment, requires hospitalization
G4. Dyspepsia (heartburn)	Transient, intermittent, responds to OTC antacids, H-2 blockers	Prolonged, recurrent, requires prescription meds, relieved by meds	Persistent despite treatment, interferes with function, associated with GI bleeding	NA

G. Gastrointestinal (Continued)				
G5. GI bleed (gastritis, gastric or duodenal ulcer diagnosed-define aetiology)	Asymptomatic, endoscopic finding, haemocult + stools, no transfusion, responds rapidly to treatment	Symptomatic, transfusion ≤ 2 units needed; responds to treatment	Haematemesis, transfusion 3 – 4 units, prolonged interference with function	Recurrent, transfusion > 4 units, perforation, requiring surgery, hospitalisation
G6. Haematochezia (rectal bleeding)	Haemorrhodial, asymptomatic, no transfusion	Symptomatic, transfusion ≤ 2 units, reversible	Recurrent, transfusion > 3 – 4 units	> 4 units, hypotension, requiring hospitalization
G7. Hepatitis	Laboratory abnormalities, asymptomatic, reversible	Symptomatic laboratory abnormalities, not interfering with function, slowly reversible	Laboratory abnormalities persistent > 2 wks, symptoms interfere with function	Progressive, hepato-renal, anasarca, pre-coma or coma
G8. Nausea, or nausea/vomiting (use diagnostic term)	Transient, intermittent, minimal interference with intake, rapid response to meds	Persistent, recurrent, requires prescription meds, intake maintained	Prolonged, interferes with daily function and nutritional intake, periodic iv fluids	Hypotensive, hospitalization, parenteral nutrition, unresponsive to out-patient management
G9. Pancreatitis	Amylase elevation, intermittent nausea/vomiting, transient, responds rapidly to treatment	Amylase elevation with abdominal pain, nausea, occasional vomiting, responsive to treatment	Severe, persistent abdominal pain with pancreatitic enzyme elevation, incomplete or slow response to treatment	Complicated by shock, haemorrhage (acute circulatory failure)
G10. Proctitis	Perianal pruritus, haemorrhoids (new onset), transient, or intermittent, relieved by OTC meds	Tenesmus or ulcerations, anal fissure, responsive to treatment, minimal interference with function	Unresponsive to treatment, marked interference with function	Mucosal necrosis with haemorrhage, infection, surgery required.
H. Musculoskeletal				
H1. Avascular necrosis	Asymptomatic MRI changes, non-progressive	MRI changes and symptoms responsive to rest and analgesia	MRI changes, symptoms requiring surgical intervention	Wheelchair bound; surgical repair not possible
H2. Arthralgia	Intermittent transient symptoms, no meds or relieved by OTC meds	Persistent or recurrent symptoms, resolve with meds, little effect on function	Severe symptoms despite meds impairs function	Debilitating, hospitalisation required for treatment

H. Musculoskeletal (Continued)				
H3. Leg cramps	Transient, intermittent, does not interfere with function	Recurrent symptoms, minimally interferes with function or sleep, responds to meds	Persistent, prolonged interference with function or sleep, partial or no response to meds	NA
H4. Myalgia	Occasional; does not interfere with function	Frequent, requires meds (non-narcotic); minor effects on function	Major change in function/lifestyle, narcotic pain meds	Debilitating, profound weakness, requires wheelchair, unresponsive to meds
I. Neuropsychiatric				
I1. Anxiety or depression (mood alteration)	Symptomatic, does not interfere with function; no meds	Frequent symptoms, responds to meds; interferes with ADL at times	Persistent, prolonged symptoms, partial or no response to meds, limits daily function	Suicidal ideation or danger to self
I2. Cerebrovascular ischaemia	NA	Single transient ischaemic event, responsive to treatment	Recurrent transient ischaemic events	Cerebrovascular vascular accident with permanent disability
I3. Cognitive disturbance	Subjective symptoms, transient, intermittent, not interfering with function	Objective symptoms, persisting, interferes with daily function occasionally	Persistent, or worsening objective symptoms; interferes with routine daily routine	Debilitating/disabling and permanent; toxic psychosis
I4. Depressed consciousness (somnolence)	Observed, transient, intermittent, not interfering with function	Somnolence or sedation, interfering with function	Persistent, progressive, obundation, stupor	Coma
I5. Inability to concentrate	Subjective symptoms, does not interfere with function	Objective findings, interferes with function	Persistent, prolonged objective findings or organic cause	NA
I6. Insomnia (in absence of pain)	Occasional difficulty sleeping, transient intermittent, not interfering with function	Recurrent difficulty sleeping; requires meds for relief; occasional interference with function	Persistent or worsening difficulty sleeping; severely interferes with routine daily function	NA
I7. Libido decreased	Decrease in interest	Loss of interest; influences relationship	Persistent, prolonged interfering with relationship	NA

I. Neuropsychiatric (Continued)				
I8. Peripheral motor neuropathy	Subjective or transient loss of deep tendon reflexes; function maintained	Objective weakness, persistent, no significant impairment of daily function	Objective weakness with substantial impairment of function	Paralysis
I9. Peripheral sensory neuropathy (sensory disturbance)	Subjective symptoms without objective findings, transient, not interfering with function	Objective sensory loss, persistent, not interfering with function	Prolonged sensory loss or paraethesias interfering with function	NA
I10. Seizure	NA	Recurrence of old seizures, controlled with adjustment of medication	Recurrence/exacerbation with partial response to medication	Recurrence not controlled, requiring hospitalization; new seizures
I11. Vertigo (dizziness)	Subjective symptoms, transient, intermittent, no treatment	Objective findings, recurrent, meds relieve, occasionally interfering with function	Persistent, prolonged, interfering with daily function; partial response to medication	Debilitating without response to medication, hospitalization
J. Pulmonary				
J1. Asthma	Occasional wheeze, no interference with activities	Wheezing, requires oral meds, occasional interference with function	Debilitating, requires nasal O_2	Requires ventilator assistance
J2. Cough	Transient, intermittent, occasional OTC meds relieve	Persistent, requires narcotic or other prescription meds for relief	Recurrent, persistent coughing spasms without consistent relief by meds, interferes with function	Interferes with oxygenation; debilitating
J3. Dyspnea	Subjective, transient, no interference with function	Symptomatic, intermittent or recurring, interferes with exertional activities	Symptomatic during daily routine activities, interferes with function, treatment with intermittent nasal O_2 relieves	Symptomatic at rest, debilitating, requires constant nasal O_2
J4. Pleuritic pain (pleurisy)	Transient, intermittent symptoms, no treatment or OTC meds relieve	Persistent symptoms, requires prescription meds for relief	Prolonged symptoms, interferes with function, requires frequent narcotic pain relief	Debilitation, requiring hospitalisation

J. Pulmonary (Continued)				
J5. Pneumonitis (pulmonary infiltrates)	Asymptomatic radiographic changes, transient, no treatment required	Symptomatic, persistent, requiring corticosteroids	Symptomatic, requiring treatment including O_2	Debilitating, not reversible; or requiring assisted ventilation
J6. Pulmonary function decreased (FVC or carbon monoxide diffusion capacity – DLCO)	76% – 90% of pre-treatment value	51% – 75% of pre-treatment value	26% – 50% of pre-treatment value	≤ 25% of pre-treatment value

Appendix T. Class VI and Class VII Topical Corticosteroid Examples

Class	Generic Name or Local Equivalent	%
VI	Prednicarbate	0.05
	Triamcinolone acetonide	0.025
	Desonide	0.05
	Fluocinolone acetonide	0.01
	Triamcinolone acetonide	0.025
	Flumethasone pivalate	0.03
	Fluocinolone acetonide	0.01
	Desonide	0.05
	Triamcinolone acetonide	0.025
	Betamethasone valerate	0.01
VII	Betamethasone valerate	0.2
	Hydrocortisone acetate	1.0
	Hydrocortisone	1.0, 2.5
	Methylprednisolone	0.25
	Fluorometholone	0.025
	Hydrocortisone	1.0, 2.5

Appendix U. Follow-up Phone Call

Site Name/Number: _____/_____

Subject Number: _____

Contact subjects that signed the protocol Amendment 1 ICF approximately 140 days (20 weeks) following last study drug administration.

Date of Call/Visit: _____

☐ Lost to Follow-up (check this box if subject was not willing to provide any follow-up information or you were unable to speak to the subject following at least two phone call attempts and one certified letter).

☐ No Events Reported

At the Follow-up Phone Call:

☐ Record any adverse events (AEs) and/or serious adverse events (SAEs) that occurred since the subject's last study visit. Document all AEs/SAEs in source records and EDC system. Report all SAEs to AbbVie within 24 hours of awareness of the event.

☐ Request update to the status of any AE that was ongoing at the last study visit.

☐ Request update to any concomitant medication(s) that was ongoing at the last study visit. Record any change in concomitant medication in source documents and EDC.

Name of person completing form (printed): _____

Signature of person completing form: _____

Date: _____

Please email this completed form to [redacted]

Appendix V. Protocol Amendment: List of Changes

The summary of changes is listed in Section 1.1.

Specific Protocol Changes

Section 1.0 Title Page
"Sponsor Contact:" previously read:

Sponsor Contact: [redacted]

Has been changed to read:

Sponsor Contact: [redacted]

Section 1.0 Title Page
"Emergency Medical Contact:," "Bldg" previously read:

Bldg AP30

Has been changed to read:

Bldg AP31

Section 1.1 Synopsis
Subsection Diagnosis and Main Criteria for Inclusion/Exclusion:
Heading "Main Inclusion:"
Criterion 2 previously read:

Women of childbearing potential who are sexually active, must agree to use at least one accepted method of contraception throughout the study, including 16 weeks after last dose of study drug is given.

Has been changed to read:

Women of childbearing potential who are sexually active, must agree to use at least one accepted method of contraception throughout the study, including 20 weeks after last dose of study drug is given.

Section 1.1 Synopsis
Subsection Diagnosis and Main Criteria for Inclusion/Exclusion:
Heading "Main Exclusion:"
Criterion 1 previously read:

Female subject who is pregnant, breastfeeding or is considering becoming pregnant during study participation, including 16 weeks after the last dose of study drug is given.

Has been changed to read:

Female subject who is pregnant, breastfeeding or is considering becoming pregnant during study participation, including 20 weeks after the last dose of study drug is given.

Section 1.2 List of Abbreviations and Definition of Terms
Subsection Abbreviations
Add:

$t_{1/2}$ Half-life

Section 3.3 Differences Statement
First sentence previously read:

Study M16-244 is a 52 week multicenter, single-arm, open-label extension (OLE), consisting of 36 weeks of study drug administration and 16 weeks follow-up, to Study 1311.5.

Has been changed to read:

Study M16-244 is a 52 week multicenter, single-arm, open-label extension (OLE), consisting of 36 weeks of study drug administration and 20 weeks follow-up, to Study 1311.5.

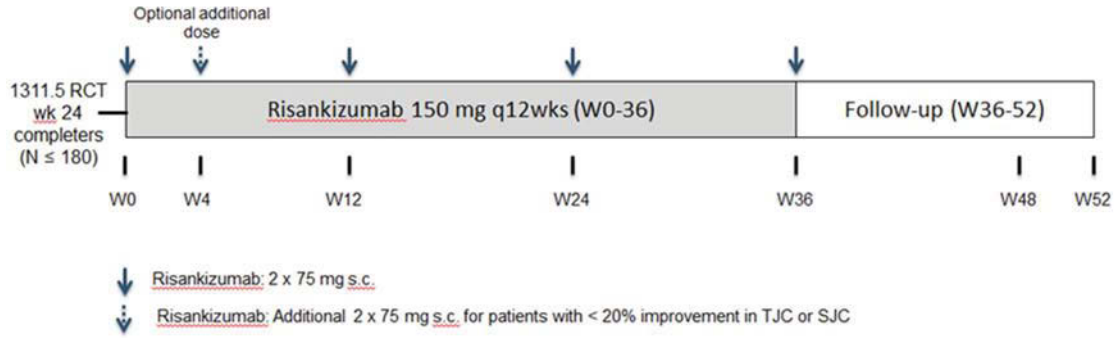
Section 5.1 Overall Study Design and Plan: Description
Subsection Follow-Up Period
First paragraph previously read:

Subjects will have follow-up visits at Week 48 and 52. All Follow-Up Visit procedures are noted in Appendix C. Subjects who discontinue study drug treatment early will need to attend an early End of Treatment (EOT) visit ideally within 2 weeks after the decision and preferably prior to the administration of any new therapies. An additional End of Study (EOS) visit, 16 weeks after their last dose of study drug, is required to determine the status of any ongoing AEs/SAEs or the occurrence of any new AEs/SAEs (see Appendix C and Section 5.4.1).

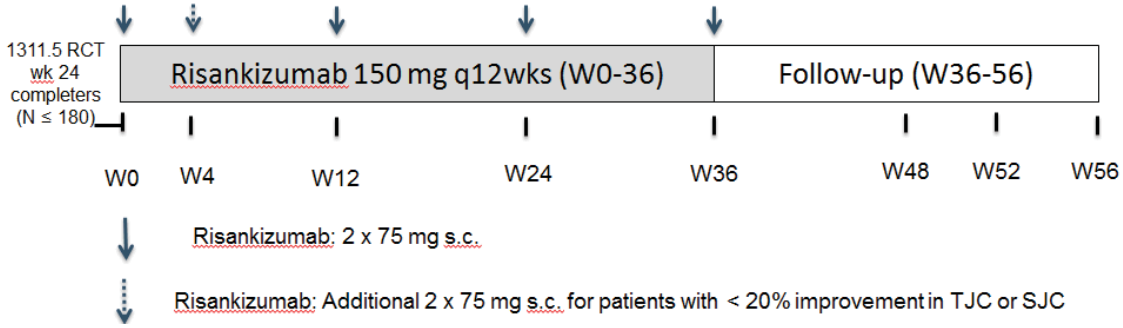
Has been changed to read:

Subjects will have follow-up visits at Week 48 and 52 and a Follow-up Phone call 20 weeks after the last dose of study drug. All Follow-up Visit procedures are noted in Appendix C. Subjects who discontinue study drug treatment early will need to attend an early End of Treatment (EOT) visit ideally within 2 weeks after the decision and preferably prior to the administration of any new therapies. An End of Study (EOS) visit 16 weeks after the last dose of study drug and a Follow-up Phone Call 20 weeks after the last dose of study drug is required to determine the status of any ongoing AEs/SAEs or the occurrence of any new AEs/SAEs (see Appendix C and Section 5.4.1).

Figure 2. Study M16-244 Study Design
Previously read:



Has been changed to read:



Section 5.2.1 Inclusion Criteria
Criterion 2 previously read:

Women of childbearing potential must agree to use at least one of the following methods of contraception throughout the study including 16 weeks after the last study drug dose is given.

Has been changed to read:

Women of childbearing potential must agree to use at least one of the following methods of contraception throughout the study including 20 weeks after the last study drug dose is given.

Section 5.2.2 Exclusion Criteria
Criterion 1 previously read:

Female subject who is pregnant, breastfeeding or is considering becoming pregnant during study participation, including 16 weeks after the last dose of study drug is given.

Has been changed to read:

Female subject who is pregnant, breastfeeding or is considering becoming pregnant during study participation, including 20 weeks after the last dose of study drug is given.

Section 5.2.4 Contraception Recommendations and Pregnancy
First paragraph, last sentence previously read:

The method chosen must be practiced throughout the study including 16 weeks after the last dose of study drug is given.

Has been changed to read:

The method chosen must be practiced throughout the study including 20 weeks after the last dose of study drug is given.

Section 5.4.1 Discontinuation of Individual Subjects
First bullet previously read:

A subject does not attain a protocol defined (defined as an improvement in tender and swollen joint count of ≥ 20% compared with the baseline in Study 1311.5) at 2 consecutive visits at Week 12 visit, or thereafter.

Has been changed to read:

A subject does not attain a protocol defined response (defined as an improvement in tender and swollen joint count of ≥ 20% compared with the baseline in Study 1311.5) at 2 consecutive visits at Week 12 visit, or thereafter.

Section 5.4.1 Discontinuation of Individual Subjects
Third paragraph, last sentence previously read:

For subjects that prematurely discontinue, study drug will not be given at the early EOT visit and subjects should attend their EOS Visit 16 weeks after last study drug dose to determine the status of any ongoing AEs/SAEs or the occurrence of any new AEs/SAEs (see Appendix C).

Has been changed to read:

For subjects that prematurely discontinue, study drug will not be given at the early EOT visit and subjects should attend their EOS Visit 16 weeks after last study drug dose and complete a Follow-up Phone Call 20 weeks after the last dose of study drug to determine the status of any ongoing AEs/SAEs or the occurrence of any new AEs/SAEs (see Appendix C).

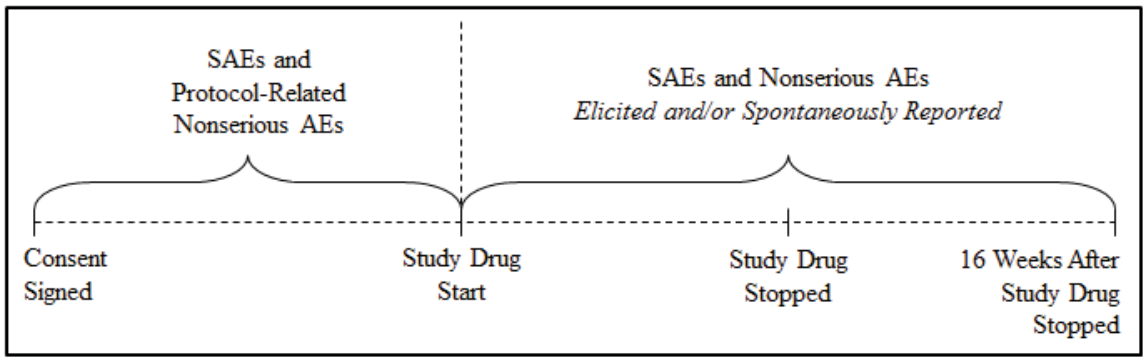
Section 6.1.4 Adverse Event Collection Period
First paragraph, first sentence previously read:

All adverse events reported from the time of study drug administration until 16 weeks, following discontinuation of study drug administration have elapsed will be collected, whether solicited or spontaneously reported by the subject.

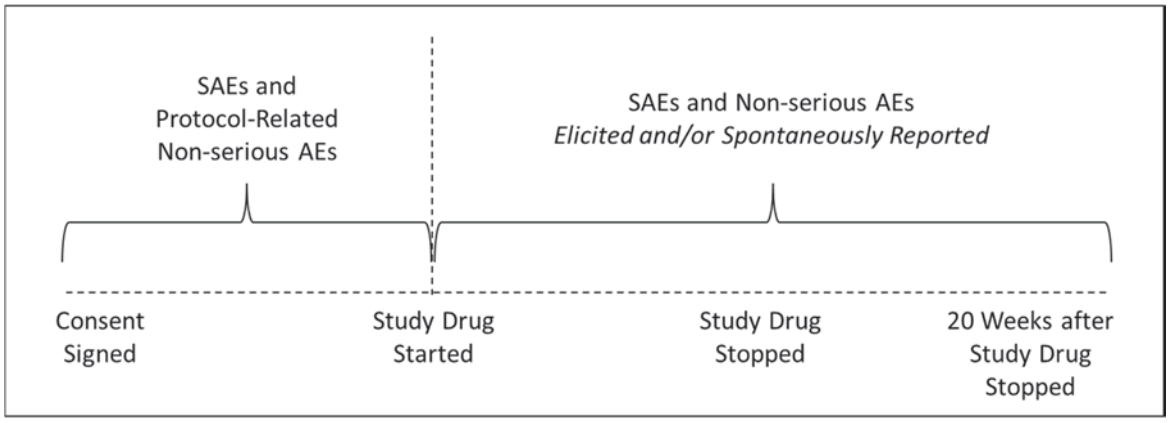
Has been changed to read:

All adverse events reported from the time of study drug administration until 20 weeks, following discontinuation of study drug administration have elapsed will be collected, whether solicited or spontaneously reported by the subject.

Figure 3. Adverse Event Collection
Previously read:



Has been changed to read:



Section 6.1.5 Adverse Event Reporting
"Primary Therapeutic Area Medical Director:," "Bldg" previously read:

Bldg AP30

Has been changed to read:

Bldg AP31

Section 7.0 Protocol Deviations
"Alternate Contact:" previously read:

Has been changed to read:

Section 8.1.6.2.1 Treatment-Emergent Adverse Events
First paragraph, last sentence previously read:

AEs starting more than 105 days following the last dose of study drug will not be included in summaries of TEAEs

Has been changed to read:

AEs starting more than 140 days following the last dose of study drug will not be included in summaries of TEAEs.

Section 13.0 Completion of the Study
Fourth paragraph previously read:

The end-of-study is defined as the date of the last subject's last visit, 16 weeks after the final dose of study drug, see Appendix C.

Has been changed to read:

The EOS is defined as the date of the last subject's last scheduled visit or the date of the Follow-up Phone Call, whichever is later, see Appendix C.

Appendix B. List of Protocol Signatories
Previously read:

Name	Title	Functional Area
[redacted]		Clinical
		Clinical
		Statistics
		Pharmacokinetics
		BioAnalytics
		Clinical

Has been changed to read:

Name	Title	Functional Area
[redacted]		Clinical
		Clinical
		Statistics
		Pharmacokinetics
		Clinical
		Medical Writing

Appendix C. Study Activities
Previously read:

	Treatment					Follow-Up	
	V1	**V2**	**V3**	**V4**	**V5 (EOT/Early EOT[s])**	**V6**	**EOS (EOT/Early EOT + 16 Weeks)**
Week	**0[a]**	**4[t]**	**12**	**24**	**36**	**48**	**52**
Day	**1**	**29 ± 4**	**85 ± 4**	**169 ± 4**	**253 ± 4**	**336 ± 4**	**365 ± 4**
Informed Consent[b]	X						
Inclusion/exclusion criteria	X						
Medical/Surgical History[c]	X[a]						
Patient's Global Assessment of Disease Activity (VAS) (PtGA)[d]	X[a]	X	X	X	X	X	X
Patient's Assessment of PsA Pain Intensity (VAS)[d]	X[a]	X	X	X	X	X	X
HAQ-DI[d]	X[a]	X	X	X	X	X	X
BASDAI[d,m]	X[a]			X	X	X	X
SF-36v2[d]	X[a]	X	X	X	X	X	X
FACIT-F[d]	X[a]			X	X	X	
Vital Signs[e]	X[a]	X	X	X	X	X	X
ECG[e]	X[a]			X		X	X
Physical Exam[e] (c = complete, t = targeted)	X-c[a]	X-t	X-t	X-t	X-t	X-t	X-c

	Treatment					Follow-Up	
	V1	**V2**	**V3**	**V4**	**V5 (EOT/Early EOT[s])**	**V6**	**EOS (EOT/Early EOT + 16 Weeks)**
Week	**0[a]**	**4[t]**	**12**	**24**	**36**	**48**	**52**
Day	**1**	**29 ± 4**	**85 ± 4**	**169 ± 4**	**253 ± 4**	**336 ± 4**	**365 ± 4**
Concomitant Therapy[f]	X[a]	X	X	X	X	X	X
Adverse Event Assessment[g]	X[a]	X	X	X	X	X	X
Tender Joint Count (TJC 68)[h]	X[a]	X	X	X	X	X	X
Swollen Joint Count (SJC 66)[h]	X[a]	X	X	X	X	X	X
PASI[h,u]	X[a]	X	X	X	X	X	X
BSA[h]	X[a]	X	X	X	X	X	X
Static Physician's Global Assessment for Psoriasis (sPGA)[h,u]	X[a]	X	X	X	X	X	X
Physician's Global Assessment of Disease Activity (PhGA) (VAS)[h]	X[a]	X	X	X	X	X	X
Leeds Dactylitis Index (LDI)[h]	X[a]		X	X	X	X	X
Leeds Enthesitis Index (LEI)[h]	X[a]		X	X	X	X	X
SPARCC[h]	X[a]		X	X	X	X	X
mNAPSI[h]	X[a]		X	X	X	X	X
mTSS (X-ray)[i]				X		X	
Pregnancy Test[j]	X[a]	X	X	X	X	X	X

	Treatment					Follow-Up	
	V1	**V2**	**V3**	**V4**	**V5 (EOT/Early EOT[s])**	**V6**	**EOS (EOT/Early EOT + 16 Weeks)**
Week	**0[a]**	**4[t]**	**12**	**24**	**36**	**48**	**52**
Day	**1**	**29 ± 4**	**85 ± 4**	**169 ± 4**	**253 ± 4**	**336 ± 4**	**365 ± 4**
Safety Labs (Chemistry, Hematology, Urinalysis)[k,v]	X[a]	X	X	X	X	X	X
hsCRP for DAS[k]	X[a]	X	X	X	X	X	X
Blood Sample for PK[k,l]	X[a]	X	X	X	X	X	X
Blood Sample for ADA Assay[k,l]	X[a]	X	X	X	X	X	X
TB screening[k,n]				X			X[r]
Local tolerability[o]	X	X	X	X	X		
Study drug administration	X	X[p] (additional)	X	X	X		
Monitoring for hypersensitivity reaction[q]	X	X	X	X	X		
Conclusion of Subject participation							X

Has been changed to read:

	Treatment					Follow-Up		
	V1	**V2**	**V3**	**V4**	**V5 (EOT/Early EOT[s])**	**V6**	**EOS (EOT/Early EOT + 16 Weeks)**	**Follow-up Phone Call**
Week	**0[a]**	**4[t]**	**12**	**24**	**36**	**48**	**52**	**56**
Day	**1**	**29 ± 4**	**85 ± 4**	**169 ± 4**	**253 ± 4**	**336 ± 4**	**365 ± 4**	**392 ± 4**
Informed Consent[b]	X							
Inclusion/exclusion criteria	X							
Medical/Surgical History[c]	X[a]							
Patient's Global Assessment of Disease Activity (VAS) (PtGA)[d]	X[a]	X	X	X	X	X	X	
Patient's Assessment of PsA Pain Intensity (VAS)[d]	X[a]	X	X	X	X	X	X	
HAQ-DI[d]	X[a]	X	X	X	X	X	X	
BASDAI[d,m]	X[a]			X	X	X	X	
SF-36v2[d]	X[a]	X	X	X	X	X	X	
FACIT-F[d]	X[a]			X	X	X		
Vital Signs[e]	X[a]	X	X	X	X	X	X	
ECG[e]	X[a]			X		X	X	
Physical Exam[e] (c = complete, t = targeted)	X-c[a]	X-t	X-t	X-t	X-t	X-t	X-c	
Concomitant Therapy[f]	X[a]	X	X	X	X	X	X	X

	Treatment					Follow-Up		
	V1	**V2**	**V3**	**V4**	**V5 (EOT/Early EOT[$])**	**V6**	**EOS (EOT/Early EOT + 16 Weeks)**	**Follow-up Phone Call**
Week	**0[a]**	**4[t]**	**12**	**24**	**36**	**48**	**52**	**56**
Day	**1**	**29 ± 4**	**85 ± 4**	**169 ± 4**	**253 ± 4**	**336 ± 4**	**365 ± 4**	**392 ± 4**
Adverse Event Assessment[g]	X[a]	X	X	X	X	X	X	X
Tender Joint Count (TJC 68)[h]	X[a]	X	X	X	X	X	X	
Swollen Joint Count (SJC 66)[h]	X[a]	X	X	X	X	X	X	
PASI[h,u]	X[a]	X	X	X	X	X	X	
BSA[h]	X[a]	X	X	X	X	X	X	
Static Physician's Global Assessment for Psoriasis (sPGA)[h,u]	X[a]	X	X	X	X	X	X	
Physician's Global Assessment of Disease Activity (PhGA) (VAS)[h]	X[a]	X	X	X	X	X	X	
Leeds Dactylitis Index (LDI)[h]	X[a]		X	X	X	X	X	
Leeds Enthesitis Index (LEI)[h]	X[a]		X	X	X	X	X	
SPARCC[h]	X[a]		X	X	X	X	X	
mNAPSI[h]	X[a]		X	X	X	X	X	
mTSS (X-ray)[i]				X		X		
Pregnancy Test[j]	X[a]	X	X	X	X	X	X	
Safety Labs (Chemistry, Hematology, Urinalysis)[k,v]	X[a]	X	X	X	X	X	X	

	Treatment					Follow-Up		
	V1	**V2**	**V3**	**V4**	**V5 (EOT/Early EOT[s])**	**V6**	**EOS (EOT/Early EOT + 16 Weeks)**	**Follow-up Phone Call**
Week	**0[a]**	**4[t]**	**12**	**24**	**36**	**48**	**52**	**56**
Day	**1**	**29 ± 4**	**85 ± 4**	**169 ± 4**	**253 ± 4**	**336 ± 4**	**365 ± 4**	**392 ± 4**
hsCRP for DAS[k]	X[a]	X	X	X	X	X	X	
Blood Sample for PK[k,l]	X[a]	X	X	X	X	X	X	
Blood Sample for ADA Assay[k,l]	X[a]	X	X	X	X	X	X	
TB screening[k,n]				X			X[r]	
Local tolerability[o]	X	X	X	X	X			
Study drug administration	X	X[p] (additional)	X	X	X			
Monitoring for hypersensitivity reaction[q]	X	X	X	X	X			
Conclusion of Subject participation								X

Appendix D. Local Requirements
Subsection Local Requirements – Japan
Heading "Section 7.0: Protocol Deviations"
"Alternate Contact:" previously read:

[redacted]

Has been changed to read:

[redacted]

Appendix D. Local Requirements
Subsection Local Requirements – Japan
Heading "Appendix C: Study Activities Table"
Table previously read:

	Treatment					Follow-Up	
	V1	V2	V3	V4	V5 (EOT/Early EOT)	V6	EOS (EOT/Early EOT + 16 Weeks)
Week	**0**	**4**	**12**	**24**	**36**	**48**	**52**
Day	**1 ± 4**	**29 ± 4**	**85 ± 4**	**169 ± 4**	**253 ± 4**	**336 ± 4**	**365 ± 4**
HBV DNA*	X			X			X

Has been changed to read:

	Treatment					Follow-Up		
	V1	V2	V3	V4	V5 (EOT/Early EOT)	V6	EOS (EOT/Early EOT + 16 Weeks)	Follow-up Phone Call
Week	**0**	**4**	**12**	**24**	**36**	**48**	**52**	**56**
Day	**1 ± 4**	**29 ± 4**	**85 ± 4**	**169 ± 4**	**253 ± 4**	**336 ± 4**	**365 ± 4**	**365 ± 4**
HBV DNA*	X			X			X	

Appendix J. Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index
Subsection Enthesitis Count
Previously read:

Tenderness on examination is recorded as either present (1) or absent (0) for each of the 18 sites, for an overall score range of 0 – 16.

Has been changed to read:

Tenderness on examination is recorded as either present (1) or absent (0) for each of the 16 sites, for an overall score range of 0 – 16.

Appendix U. Follow-up Phone Call
Add: new appendix title and text

Appendix U. Follow-up Phone Call

Site Name/Number: _____/_____

Subject Number: _____

Contact subjects that signed the protocol Amendment 1 ICF approximately 140 days (20 weeks) following last study drug administration.

Date of Call/Visit: _____

☐ Lost to Follow-up (check this box if subject was not willing to provide any follow-up information or you were unable to speak to the subject following at least two phone call attempts and one certified letter).

☐ No Events Reported

At the Follow-up Phone Call:

☐ Record any adverse events (AEs) and/or serious adverse events (SAEs) that occurred since the subject's last study visit. Document all AEs/SAEs in source records and EDC system. Report all SAEs to AbbVie within 24 hours of awareness of the event.

☐ Request update to the status of any AE that was ongoing at the last study visit.

☐ Request update to any concomitant medication(s) that was ongoing at the last study visit. Record any change in concomitant medication in source documents and EDC.

Name of person completing form (printed): _____

Signature of person completing form: _____

Date: _____

Please email this completed form to [redacted]

Document Approval

Study M16244 - Phase 2 Single-Arm Open-Label Extension Study to Investigate Safety with Risankizumab in Psoriatic Arthritis Subjects Who Have Completed Week 24 Visit of Study 1311.5 - Amendment 1 - EudraCT 2016-003113-94 - 23May2018

Version: 1.0 **Date:** 23-May-2018 10:47:52 PM **Company ID:** 05232018-00F9F683D693F4-00001-en

Signed by:	Date:	Meaning Of Signature:
[redacted]	23-May-2018 04:18:00 PM	Approver
	23-May-2018 04:28:13 PM	Author
	23-May-2018 06:17:34 PM	Approver
	23-May-2018 09:30:29 P	Approver
	23-May-2018 10:38:23 PM	Approver
	23-May-2018 10:47:51 PM	Approver