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Protocol for Study M16-005

Plaque Psoriasis: Usability of the Risankizumab Autoinjector Combination Product in Adults with Moderate to Severe Psoriasis

VERSION:	3.0	DATE:	20 March 2019
SPONSOR:	AbbVie Inc.*	NUMBER OF SITES:	Approximately 35
ABBVIE INVESTIGATIONAL PRODUCT:	Risankizumab		

FULL TITLE: A Multicenter, Single-Arm, Open Label, Assessor-Blinded Study to Assess the Usability of the Risankizumab Autoinjector Combination Product in Adult Patients with Moderate to Severe Plaque Psoriasis

PRINCIPAL INVESTIGATOR(S): Investigator information on file at AbbVie.

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1 SYNOPSIS

Title: A Multicenter, Single-Arm, Open Label, Assessor-Blinded Study to Assess the Usability of the Risankizumab Autoinjector Combination Product in Adult Patients with Moderate to Severe Plaque Psoriasis	
Background and Rationale:	This study is being conducted to provide support for registration of the combination product risankizumab 150 mg/mL autoinjector (AI). This study will include the same drug administration schedule used in the Phase 3 pivotal trials.
Objective(s) and Endpoint(s):	The objectives of this study are to evaluate the usability of the combination product of risankizumab in an AI and to evaluate the efficacy, safety, and tolerability of risankizumab 150 mg/mL administered by AI for the treatment of adult patients with moderate to severe plaque psoriasis. The following key endpoints will be evaluated: • Proportion of subjects with an Observer rating of successful subject self-administration, defined as any subjects who successfully completed the sequence of 4 critical steps in the Instructions for Use (IFU) without errors to administer study drug via the AI at Week 0 and Week 28 • Proportion of subjects achieving at least 90% improvement from baseline in the Psoriasis Area and Severity Index (PASI) (PASI 90) at Week 16 • Proportion of subjects achieving sPGA clear or almost clear at Week 16
Investigator(s):	Investigator information on file at AbbVie
Study Site(s):	Approximately 35 sites in the United States
Study Population and Number of Subjects to be Enrolled:	Approximately 100 adult subjects with moderate to severe plaque psoriasis
Investigational Plan:	This is a Phase 3 multicenter, single-arm, open-label study that will evaluate usability of the risankizumab-AI combination product. In addition, efficacy will be evaluated by a study treatment assessor. The study includes a 30-day screening period with study visits at Week 0, 4, 16, 28, and 40 with a subsequent follow up telephone call at approximately 20 weeks (140 days) after the last dose of study drug (Week 48). Study drug dosing will consist of four self-administered doses given subcutaneously on Weeks 0, 4, 16, and 28. Subjects will be instructed at Week 0 (pre-injection) by the site staff on how to self-inject via the AI. The Week 0 and Week 28 usability assessments will take place in the context of an observed assessment under the supervision of one site staff member. Site staff will assess potential use-related hazards with a predefined possible hazards checklist. Dosing on Week 4 and Week 16 will be self-administered at home. Efficacy assessments will be performed at each study visit (Weeks 0, 4, 16, 28, and 40).

Key Eligibility Criteria:	Adult male or female subjects with stable moderate to severe plaque psoriasis, defined as ≥ 10% BSA psoriasis involvement, sPGA score of ≥ 3, and PASI ≥ 12 at Screening and baseline visit.
Study Drug and Duration of Treatment:	Risankizumab 150 mg at Weeks 0, 4, 16, and 28.
Date of Protocol Synopsis:	20 March 2019

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2 INTRODUCTION

2.1 Background and Rationale

Why Is This Study Being Conducted

Risankizumab is a fully humanized monoclonal antibody (mAb) of the immunoglobin G1 subclass directed towards interleukin (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.

Positive results were observed from 4 pivotal Phase 3 clinical trials that evaluated risankizumab compared with ustekinumab, placebo, and adalimumab for the treatment of patients with moderate to severe plaque psoriasis. Results from these pivotal studies demonstrated that risankizumab is highly effective for the treatment of psoriasis, meeting co-primary endpoints of achieving at least a 90% improvement in the Psoriasis Area and Severity Index (PASI 90) and static physician global assessment (sPGA) score of clear or almost clear (0 or 1) versus comparator or placebo at Week 16 across all 4 studies.[1]

In the pivotal Phase 3 clinical trials, the risankizumab 150-mg dose was administered with a 90-mg/mL formulation via 2 subcutaneous (SC) 75-mg injections. To deliver a more patient-friendly experience, a new formulation was developed at 150 mg/mL that will enable delivery of the 150 mg dose with one SC injection. This study will evaluate the risankizumab 150-mg/mL formulation self-administered by AI using the same dosing regimen of risankizumab (150 mg dose at Week 0, Week 4, and every 12 weeks thereafter) as used in the Phase 3 pivotal trials for psoriasis.

Clinical Hypothesis

No formal hypothesis test will be performed. Summary data will be used to evaluate usability.

2.2 Benefits and Risks to Subjects

In Phase 1 and Phase 2 studies of risankizumab in patients with psoriasis, the majority of subjects receiving risankizumab achieved 90% improvement of their disease, and risankizumab was well tolerated. As with many immune modulating agents, risankizumab may impair immune function resulting in a risk of infection. This will be monitored by collection of all adverse events (AEs) during the treatment and observation periods. In addition, subjects with active infection will not be included in the study.

Subjects with a positive QuantiFERON®-test or a positive purified protein derivative (PPD) skin test for tuberculosis (TB) must fulfill entry criteria as specified in Section 5.1 of this protocol. Interleukin-23 inhibition is not known to increase the risk of TB infection or impair the response to TB infection in animal models.[2,3] There have been no cases of active TB, including no reactivation of TB in subjects diagnosed with latent TB, across the entire risankizumab development program. Across the Phase 3 psoriasis clinical studies, of the 72 subjects with latent TB who were concurrently treated with risankizumab and appropriate TB prophylaxis during the study, none developed active TB during a mean

follow-up of 61 weeks on risankizumab. Of the 33 subjects in Study M15-992 with a positive test for latent TB and who did not receive prophylaxis during the study, none developed active TB during the mean follow-up of 77 weeks on risankizumab.

Thus, low risk subjects with positive QuantiFERON testing do not need to be treated with anti-TB therapy prior to receiving risankizumab, but should be carefully monitored for any sign of TB reactivation. Absence of TB reactivation, despite not receiving anti-TB prophylaxis, will provide important information in humans as to whether TB testing is required prior to treatment with risankizumab.[4]

Published literature indicates that inhibition of IL-23 is unlikely to increase the risk for cancer. Expression of IL-23 is increased in human tumors. Preclinical data have moreover demonstrated beneficial effect of IL-23 p19 inhibition in animal models, both for pre-existing and tumor-induction models. However, there is not enough clinical information at this time to rule out a risk of cancer with risankizumab, but this risk is considered small.

Although rare, a potential for hepatic adverse events is under constant surveillance by sponsors and regulators. Therefore, this study requires timely detection, evaluation, and follow-up of laboratory alterations in selected liver laboratory parameters to ensure subjects' safety.

Increases in major adverse cardiovascular (MACE) events including myocardial infarction, cerebrovascular accident, and cardiovascular death, reported initially with anti-IL-12/23 agents, such as ustekinumab, have not been observed in longer term studies. While the likelihood of increased MACE is small, all suspected cardiovascular events (serious or nonserious) observed in this study will be adjudicated by an independent adjudication committee. An independent Cardiovascular Adjudication Committee (CAC) will adjudicate all observed cardio- and cerebro-vascular events and will remain blinded to treatment allocation (Section 6.2).

Injection-site reactions to biologic therapies may be characterized by redness, swelling, or induration at the injection site. Manifestations of anaphylaxis may include pruritus, hypotension, swollen lips and tongue, abdominal pain, and respiratory distress. Both local and systemic hypersensitivity reactions and anaphylaxis are readily detectable, transient in nature, and manageable with standard medical treatment. Subjects will be closely monitored on site during study drug administration at Weeks 0 and 28. The duration of the post-drug-administration safety surveillance is 2 hours post-first dose and 1 hour postdose at Week 28. Subjects will be given instructions regarding management of signs and symptoms of anaphylaxis to be followed during home dosing at Weeks 4 and 16. An independent Anaphylaxis Adjudication Committee (AAC) will adjudicate suspected anaphylactic reactions. The AAC will remain blinded to treatment allocation (Section 6.3).

In conclusion, the benefit-risk profile of risankizumab is considered appropriate for this stage of clinical development. Based on data from the integrated safety analyses, risankizumab is safe and well tolerated and demonstrates a favorable benefit-risk profile. For further details, please see findings from completed studies, including safety data in the risankizumab Investigator Brochure.[1]

3 STUDY OBJECTIVES AND ENDPOINTS

3.1 Objectives

The objectives of this study are to evaluate the usability of the combination product of risankizumab in an AI, as well as to evaluate the efficacy, safety, and tolerability of risankizumab administered by AI for the treatment of adult patients with moderate to severe plaque psoriasis.

3.2 Key Study Endpoints

The following key endpoints will be evaluated:

- Proportion of subjects with an Observer rating of successful subject self-administration, defined as any subjects who successfully completed the sequence of 4 critical steps in the Instructions for Use (IFU) without errors to administer study drug via the AI at Week 0 and 28
- Proportion of subjects achieving at least 90% improvement from baseline in PASI (PASI 90) at Week 16
- Proportion of subjects achieving sPGA clear or almost clear at Week 16
- Proportion of subjects achieving 100% improvement from baseline in PASI (PASI 100) at Week 16
- Proportion of subjects achieving at least 75% improvement from baseline in PASI (PASI 75) at Week 16
- Proportion of subjects who had no potential hazards as measured by an Observer on the possible use-related hazards checklist for self-administration with AI at Week 0 and Week 28
- Subject rating of acceptability by the Self-Injection Assessment Questionnaire (SIAQ; Operations Manual Appendix B) at each visit collected.

3.3 Additional Endpoints

- Proportion of subjects achieving PASI 50/75/90/100, sPGA of clear, and sPGA of clear or almost clear, as well as change and percent change from baseline in PASI, at each visit collected.

3.4 Safety Endpoints

Safety evaluations include AE monitoring, physical examinations, vital sign measurements, and clinical laboratory testing (hematology and chemistry) as measures of safety and tolerability.

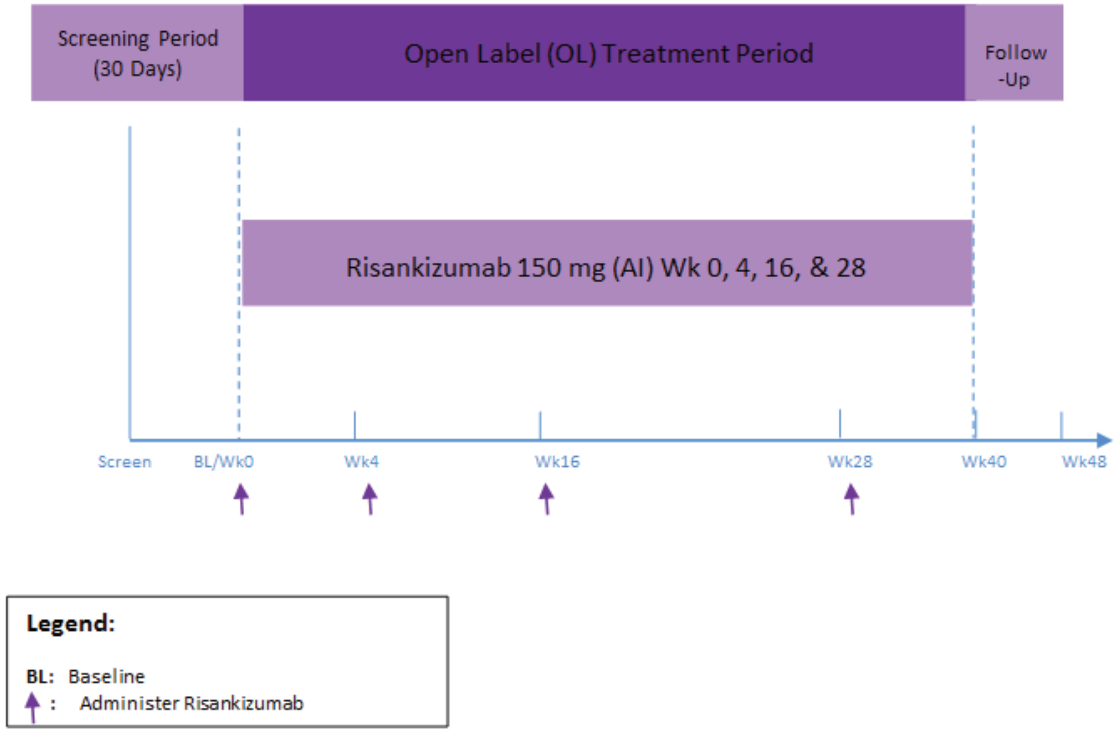
4 INVESTIGATIONAL PLAN

4.1 Overall Study Design and Plan

This is a Phase 3 multicenter, single-arm, open-label study that will evaluate usability of the risankizumab-AI combination product. In addition, efficacy will be evaluated by a study treatment assessor. The study includes a 30-day screening period with study visits at Week 0, 4, 16, 28, and 40 with a subsequent follow-up telephone call at approximately 20 weeks after the last dose of study drug (Week 48). Study drug dosing will consist of four self-administered doses given subcutaneously on Weeks 0, 4, 16, and 28. Dosing on Week 4 and Week 16 will be self-administered at home.

The schematic of the study is shown in Figure 1.

Figure 1. Study Schematic



AI = autoinjector

If an exclusionary laboratory result is obtained at the initial Screening Visit, one re-test of that particular test is allowed without repeating all other laboratory tests within the 30 day screening window.

Subjects who initially do not meet all eligibility criteria for the study may be permitted to repeat the Screening Visit one time following re-consent. The subject must meet all eligibility criteria on the repeat Screening Visit in order to qualify for the study. The repeat screening procedure is:

- A repeat of all screening procedures is needed at this repeat Screening Visit with these exceptions:
  - If the subject had a complete initial screening evaluation, including the assessment of an Interferon-Gamma Release Assay (IGRA; QuantiFERON Tuberculosis [TB] Gold In Tube test) or a PPD test (or equivalent), and electrocardiogram (ECG), these tests will not be required to be repeated at the repeat Screening Visit.
- There is no minimum period of time a subject must wait prior to the repeat Screening Visit.

Subjects will be instructed at Week 0 (pre-injection) by the site staff on how to self-inject via the AI. Self-injections will be administered into one of the following body regions, changing the injection site if possible at each time point: right thigh, left thigh, right abdominal area, left abdominal area.

At Week 0 (after training) and Week 28, subjects will be instructed by site staff to refer to the IFU (refer to Appendix E of the Operations Manual) and proceed with self-injection. At the Week 4 and Week 16 Visits, subjects will be sent home with one AI to be self-administered within 24 hours of the Week 4 and Week 16 Visit respectively, with instructions from the site staff to use the IFU. The Week 0 and Week 28 usability assessments will take place in the context of an observed assessment under the supervision of one site staff member. Each assessment is to be conducted on a 1:1 basis. The observer (site staff member) will measure and evaluate the subject's usability of the AI using the self-injection assessment checklist as they observe the injections at Week 0 and Week 28.

Site staff will assess potential use-related hazards with a predefined possible hazards checklist (refer to Appendix G of the Operations Manual) for self-injections at Week 0 and Week 28. During the self-injection, if a subject is not acting in a safe or reasonable manner the observing site staff member is required to intervene. Use errors, which could pose a risk to the health or well-being of a subject, require the observing staff member to ask the subject to pause, to point out the use error, and to decide whether to terminate the self-injection. If the observing site staff member's judgment the self-injection can continue, they should correct the subject's usage of the product and notify the subject to recommence at the same point. These errors will be documented from the list of potential use-related hazards. Any risk of a health and safety incident could result in termination of the self-injection at the discretion of the observing site staff member.

Subject-derived usability assessment measures acceptability of the AI using the SIAQ. Subjects will fill out the SIAQ PRE module (refer to Appendix B of the Operations Manual) immediately before the first self-injection at Week 0 and the POST module 20 to 40 minutes following self-injections at Week 0, Week 4, Week 16, and Week 28. These modules are to be completed by subjects while alone in a quiet environment. The subject's self-rated assessment of each item of the SIAQ, will be transformed during analysis to scores ranging from 0 (worst experience) to 10 (best experience) as described in Appendix B of the Operations Manual.

At Week 0, after the subject self-injects, the site will collect the used AI and examine them for technical performance. The site will document the result in the appropriate eCRF.

See Section 5 for information regarding eligibility criteria.

Further details regarding study procedures are located in the Operations Manual.

An interim analysis will occur after all ongoing subjects complete the Week 28 Visit. Efficacy assessors will remain blinded for the duration of the study.

4.2 Discussion of Study Design

Choice of Control Group

This is an open-label study. There is no control group.

Appropriateness of Measurements

Standard statistical, efficacy, and safety procedures will be utilized in this study. All efficacy measurements in this study are standard for assessing disease activity in subjects with moderate to severe plaque psoriasis. All clinical and laboratory procedures in this study are standard and generally accepted.

The SIAQ evaluates patients' experiences with self-injection and enables assessment of their success in giving self-injections and the likelihood of them adhering to a self-injection regimen.[5] It has been validated in patients with rheumatoid arthritis and measured in patients with psoriasis and psoriatic arthritis.[6-8]

Suitability of Subject Population

Subjects who have moderate to severe plaque psoriasis, defined as a PASI score ≥ 12, body surface area (BSA) involvement ≥ 10%, and sPGA ≥ 3 who are candidates for systemic therapy are eligible for this study. Criteria such as laboratory values (minimums and maximums) and subject history (absence of chronic infections such as human immunodeficiency virus [HIV], hepatitis B or C [HBV, HCV]), and other exclusions are specified to ensure subject safety and to allow adequate evaluation of the study drug. The study population selected reflects a standard population for moderate to severe psoriasis trials with new treatment intervention.

Selection of Doses in the Study

The risankizumab dosing regimen selected for the current study is the same as used in the risankizumab pivotal Phase 3 studies in subjects with moderate to severe chronic plaque psoriasis. Risankizumab has been found to be safe and well tolerated with no dose limiting safety findings following single- or multiple-dose administration at doses up to [redacted] mg SC or 1800 mg intravenously in Phase 1 to 3 clinical studies.[1]

Blinded Efficacy Assessor

A qualified physician (may be a non-dermatologist) or designee (may be a non-physician) from the site will be responsible for performing the efficacy assessments, including PASI, BSA, and sPGA at all appropriate study visits (Table 1). The site will make every attempt to have the same qualified physician or designee perform these assessments throughout the study for each subject. The efficacy assessor must remain blinded to patient's treatment, clinical laboratory results, and all subject safety data during

the course of the study. The efficacy assessor will not view or discuss any subject specific safety data with the investigators or any other site personnel, with the exception of the dermatologic safety findings requiring urgent medical attention. The efficacy assessor therefore cannot be the Principal Investigator. The efficacy assessor will not access patient's electronic case report form (eCRF) and will document the dermatologic assessments and potential dermatologic safety findings on paper worksheets that will be filed as source in the patient's record. It is recommended that each study site has a designated back-up for the efficacy assessor.

Table 1. Tasks of the Efficacy Assessor and Investigator

Activities	Responsible Party
Assesses PASI, BSA, sPGA	Efficacy Assessor[a]
Looks for any potential dermatologic safety finding	Efficacy Assessor
Documents the efficacy assessments and any potential safety findings on worksheets	Efficacy Assessor
Assesses safety	Investigator
Knows treatment allocation	Investigator
Reviews laboratory data	Investigator
Conduct the complete and any targeted physical examinations[b]	Investigator
Completes the CRF	Investigator, unblinded study team
Documents findings in the e-CRF	Investigator, unblinded study team
Reports information about safety findings[c]	Investigator

a. The efficacy assessor is a physician or a designee that is blinded to all aspects of the study other than the efficacy assessments.

b. The investigator will also look for potential dermatologic safety findings.

c. If the efficacy assessor identifies a safety issue this will be transmitted to the investigator over the worksheet. Dermatologic safety findings requiring urgent medical attention will be the only safety issues that the efficacy assessor may discuss with the investigator.

5 STUDY ACTIVITIES

5.1 Eligibility Criteria

Subjects must meet all of the following criteria to be included in the study. Anything other than a positive response to the questions below will result in exclusion from study participation.

Consent

- 1. Subjects or their legally authorized representative 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 screening or study-specific procedures.

Demographic and Laboratory Assessments

- 2. Adult **male or female**, at least 18 years old.
- 3. **Laboratory values** meeting the following criteria within the screening period prior to the first dose of study drug:
  - Serum aspartate transaminase < 2 × upper limit of normal (ULN);
  - Serum alanine transaminase < 2 × ULN;
  - Serum direct bilirubin ≤ 2.0 mg/dL; except for subjects with isolated elevation of indirect bilirubin relating to a confirmed diagnosis of Gilbert syndrome;
  - Total white blood cell count > 3,000/µL;
  - Absolute neutrophil count > 1,500/µL;
  - Platelet count > 100,000/µL;
  - Hemoglobin > 8 g/dL.
- 4. Are willing or able to comply with procedures required in this protocol including self-administration of study drug.

Disease Activity

- 5. Diagnosis of chronic plaque psoriasis for at least 6 months before the baseline visit.
- 6. Subject meets the following disease activity criteria:
  - Stable moderate to severe chronic plaque psoriasis, defined as ≥ 10% BSA psoriasis involvement, sPGA score of ≥ 3, and PASI ≥ 12 at Screening and baseline visit;
  - Candidate for systemic therapy as assessed by the investigator;

Subject History

- 7. No history of:
  - Erythrodermic psoriasis, generalized or localized pustular psoriasis, medication-induced or medication-exacerbated psoriasis, or new onset guttate psoriasis;
  - Active skin disease other than psoriasis that could interfere with the assessment of psoriasis;
  - Chronic infections including human immunodeficiency virus, viral hepatitis (hepatitis B, hepatitis C), and/ or active TB. Subjects with a positive QuantiFERON®-TB /purified protein

derivative (tuberculin) test result may participate in the study if further work up (according to local practice/guidelines) establishes conclusively that the subject has no evidence of active TB. If presence of latent TB is established, subjects are not required to be treated with prophylactic anti-TB therapy prior to or during the study, if the subject is considered low risk for reactivation per investigator judgment.

- Active systemic infection during the last 2 weeks prior to baseline visit (exception: common cold), as assessed by the investigator.

8. No history of any documented active or suspected malignancy or history of any malignancy within the last 5 years except for successfully treated non-melanoma skin cancer or localized carcinoma in situ of the cervix.

9. No history of clinically significant (per investigator's judgment) **drug or alcohol abuse** within the last 6 months.

10. No history of underlying medical diseases or problems including but not limited to the following:

- Subject has been a previous recipient of a solid organ transplant;
- Evidence of a current or previous disease, medical condition (including chronic alcohol or drug abuse) other than psoriasis, surgical procedure (i.e., organ transplant), medical examination finding (including vital signs and electrocardiogram), or laboratory value at the screening visit outside the given range that, in the opinion of the investigator, is clinically significant and would make the study participant unreliable to adhere to the protocol or to complete the trial, compromise the safety of the patient, or compromise the quality of the data;

11. No history of an **allergic reaction** or significant sensitivity to constituents of the study drug (and its excipients) and/or other products in the same class.

12. No major surgery performed within 12 weeks prior to randomization or planned to be performed during the conduct of the trial (e.g., hip replacement, aneurysm removal, stomach ligation) as assessed by the Investigator.

Contraception

13. For all females of child-bearing potential; a **negative serum pregnancy test** at the Screening Visit and a negative urine pregnancy test at baseline and following visits (as outlined in the Study Activity Table of this protocol) prior to the first dose of study drug.

14. Female subjects must be postmenopausal OR permanently surgically sterile OR for a woman of child bearing potential be practicing at least one protocol-specified method of birth control (Section 5.2) that is effective from the baseline visit through at least 140 days (20 weeks) after the last dose of study drug

15. Female who is not **pregnant, breastfeeding, or considering becoming pregnant** during the study or for approximately 140 days (20 weeks) after the last dose of study drug.

16. Additional local requirements may apply.

Concomitant Medications

- 17. No previous exposure to risankizumab.
- 18. No use of any restricted medication as specified in the prohibited medications/therapy section or any drug considered likely to interfere with the safe conduct of the study.
- 19. Subject must not have been treated with **any investigational drug** within 30 days or 5 half-lives of the drug (whichever is longer) prior to the first dose of study drug or is currently enrolled in another clinical study.

5.2 Contraception Recommendations

Contraception Requirements for Females

Subjects must follow the following contraceptive guidelines as specified:

- Females, Non-Childbearing Potential

  Females do not need to use birth control during or following study drug treatment if considered of non-childbearing potential due to meeting any of the following criteria:

  - Postmenopausal, age > 55 years with no menses for 12 or more months without an alternative medical cause
  - Postmenopausal, age ≤ 55 years with no menses for 12 or more months without an alternative medical cause AND a follicule-stimulating hormone (FSH) level > 40 IU/L
  - Permanently surgically sterile (bilateral oophorectomy, bilateral salpingectomy, or hysterectomy)
  - Females who have not experienced menarche (at least one menstrual period)

- Females, of Childbearing Potential

  Females of childbearing potential must avoid pregnancy while taking study drug(s) and for at least 140 days after the last dose of study drug.

  Females must commit to one of the following methods of birth control:

  - Combined (estrogen and progestogen containing) hormonal birth control (oral, intravaginal, transdermal, injectable) associated with inhibition of ovulation initiated at least 1 month prior to study Baseline (Study Day 1)
  - Progestogen-only hormonal birth control (oral, injectable, implantable) associated with inhibition of ovulation initiated at least 1 month prior to study Baseline (Study Day 1)
  - Bilateral tubal occlusion/ligation (can be via hysteroscopy, provided a hysterosalpingogram confirms success of the procedure)
  - Intrauterine device (IUD)
  - Intrauterine hormone-releasing system (IUS)

- Vasectomized sexual partner(s) (the vasectomized partner[s] has received medical assessment of the surgical success and is the sole sexual partner of the study subject).
- 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.

If required per local guidelines, male or female condom with or without spermicide OR cap, diaphragm or sponge with spermicide should be used in addition to one of the birth control methods listed above (excluding true abstinence).

Contraception recommendations related to use of concomitant therapies prescribed per standard of care should be based on the local label.

5.3 Prohibited Medications and Therapy

Prohibited medications and therapy are defined as using the following prohibited concomitant psoriasis treatments within the specified timeframe prior to Baseline Visit and throughout the study.

1. Any systemic biologic to treat psoriasis:
   - Adalimumab, infliximab or biosimilar versions within 12 weeks;
   - Etanercept or biosimilar versions within 6 weeks;
   - Ixekizumab, brodalumab, secukinumab, or other IL-17 inhibitors within 16 weeks;
   - Ustekinumab, efalizumab, guselkumab, tildrakizumab, mirikizumab, or other IL-23 inhibitors within 24 weeks.
2. Systemic non-biologic therapy for psoriasis, including but not limited to cyclosporine, corticosteroids, methotrexate, oral retinoids, apremilast, and fumaric acid derivatives within 4 weeks.
3. Phototherapy treatment, laser therapy, tanning booth, or extended sun exposure that could affect disease severity or interfere with disease assessments within 4 weeks.
4. Topical psoriasis treatments, including but not limited to corticosteroids, anthralin, calcipotriene, topical vitamin D derivatives, retinoids, urea, alpha- or beta-hydroxyl acids, and medicated shampoos (for example those that contain > 3% salicylic acid, corticosteroids, coal tar or vitamin D3 analogues) within 2 weeks.
   - Exception: Subjects are allowed to use bland (containing no psoriasis treatment) emollients and shampoos and/or low potency topical corticosteroids (US Class 6 - 7) on the palms, soles, face, inframammary area, and groin only.
5. Treatment with an experimental non-biologic for psoriasis within 4 weeks or five half-lives of the drug (whichever is longer).
6. Treatment with an experimental biologic for psoriasis within 12 weeks or five half-lives of the drug (whichever is longer).

7. Receipt of any live vaccine within 6 weeks or is expected to need live vaccination during study participation, including at least 20 weeks after the last dose of study drug.

Live or attenuated vaccines are NOT allowed during the study and for 140 days after the last dose of study drug. Examples of such vaccines include but are not limited to the following:

- Live attenuated influenza
- Herpes zoster (i.e., Zostavax®)
- Rotavirus
- Varicella (chicken pox)
- Measles-mumps-rubella (MMR) or measles mumps rubella varicella (MMRV)
- Oral polio vaccine (OPV)
- Smallpox
- Yellow fever
- Bacille Calmette-Guérin (BCG)
- Oral typhoid

Vaccines that are inactivated, toxoid, or biosynthetic may be administered at any time without restrictions. Examples of common vaccines that meet these criteria include but are not limited to: injectable influenza vaccine, pneumococcal, pertussis (Tdap), and Shingrix®.

5.4 Prior and Concomitant Therapy

Stable doses of concomitant therapies for chronic conditions, for which neither the condition nor the treatment are judged to exclude the patient from participation are permissible. All concomitant medications should be carefully evaluated by the investigator, and the AbbVie clinical monitor should be contacted when there are questions regarding concomitant medications.

Subjects must be able to safely discontinue any prohibited medications 5 half-lives or 4 weeks prior to initial study drug administration. Subjects must be consented for the study prior to discontinuing any prohibited medications for the purpose of meeting study eligibility.

5.5 Withdrawal of Subjects and Discontinuation of Study

A subject will be discontinued from study drug if any of the following occurs:

- Clinically significant abnormal laboratory result(s) or AE(s) that preclude continuation of the study medication, as determined by the Investigator and the Therapeutic Area Medical Director (TA MD) (as applicable).
- The Investigator believes withdrawal from the study is in the best interest of the subject.

- The subject requests withdrawal from the study.
- Eligibility criteria violation(s) are noted after the subject started study drug, if continuation of the study drug would place the subject at risk as determined by the AbbVie TA MD, after consultation with the Investigator
- Introduction of prohibited medications and continuation of the study drug would place the subject at risk as determined by the AbbVie TA MD
- Subject develops active TB at any time during the study.
- Subject becomes pregnant while participating in the study.
- Subject is diagnosed with a malignancy. Exception: localized non-melanoma skin cancer (NMSC) or carcinoma in-situ of the cervix, where discontinuation is at the discretion of the Investigator.
- Subject is significantly noncompliant with study procedures, which would put the subject at risk for continued participation in the trial.

For subjects to be considered lost to follow-up, reasonable attempts must be made to obtain information on the subject's final status. At a minimum, 2 telephone calls must be made and 1 certified letter must be sent and documented in the subject's source documentation.

AbbVie may terminate this study prematurely, either in its entirety or at any site. The investigator may also stop the study at his/her site if he/she has safety concerns. If AbbVie terminates the study for safety reasons, AbbVie will promptly notify the investigator.

5.6 Follow-Up for Subject Withdrawal from Study

To minimize missing data for efficacy and safety assessments, subjects who prematurely discontinue study drug treatment should continue to be followed for all regularly scheduled visits, unless subjects have decided to discontinue the study participation entirely (withdrawal of informed consent). Subjects should be advised on the continued scientific importance of their data even if they discontinue treatment with study drug early.

If a subject prematurely discontinues study participation (withdrawal of informed consent), the procedures outlined for the Premature Discontinuation visit (PD visit) should be completed as soon as possible, preferably within 2 weeks. In addition, a follow-up phone call 20 weeks (140 days) after the last dose of study drug may be completed to ensure all treatment-emergent AEs/serious AEs (SAEs) have been resolved.

5.7 Study Drug

Information about the study drug used in this study is presented in Table 2.

Table 2. Description of Study Drug

Study Drug	Dosage Form	Strength	Route of Administration
Risankizumab (ABBV-066)	Solution for injection in AI	150 mg/1.0 mL (150 mg/mL)	SC injection

AI = auto-injector; SC = subcutaneous

Open-label risankizumab will be packaged in quantities sufficient to accommodate study design. Each kit will be labeled per local requirements and this label must remain affixed to the kit. 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. Risankizumab must not be frozen at any time. At the Week 4 and Week 16 visits, subjects will be provided with a cooler bag and ice pack to maintain adequate storage temperature of the study drug kit. They will also be provided with a sharps containers to allow the subjects to safely transport the used AI back to the study site after self-administration of the dose at home.

Upon receipt, study drug should be stored as specified on the label and kept in a secure location. A temperature log must be maintained for documentation. Each kit will contain a unique kit number. This kit number is assigned to a subject via interactive response technology (IRT) and encodes the appropriate study drug to be dispensed at the subject's corresponding study visit.

AbbVie will not supply drug other than risankizumab, and study drug will only be used for the conduct of this study. AbbVie provided study drug should not be substituted or alternately sourced unless otherwise directed by AbbVie.

5.8 Randomization/Drug Assignment

All subjects will receive open-label risankizumab; however, the efficacy assessor will remain blinded to each subject's treatment, clinical laboratory results, and all subject safety data during the course of the study.

In the event of a medical emergency in which the Investigator believes that knowledge of study drug treatment is required for the efficacy assessor, reasonable efforts must be made to contact the AbbVie Emergency Contact.

The date and reason that the efficacy assessor's blind was broken must be recorded in the source documentation and eCRF, as applicable.

5.9 Protocol Deviations

The investigator is responsible for complying with all protocol requirements, written instructions, and applicable laws regarding protocol deviations. Protocol deviations are prohibited except when necessary to eliminate an immediate hazard to study subjects. If a protocol deviation occurs (or is

identified), the investigator is responsible for notifying IEC/IRB, regulatory authorities (as applicable), and AbbVie.

6 SAFETY CONSIDERATIONS

6.1 Complaints and Adverse Events

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. Complaints associated with any component of this investigational product must be reported to AbbVie.

Product Complaint

A product complaint is any complaint 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 (e.g., printing illegible), missing components/product, device not working properly, or packaging issues.

Product Complaints concerning the investigational product and/or device must be reported to AbbVie 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 AbbVie (or an authorized representative) and documented in source as required by AbbVie. 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. 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.

Medical Complaints/Adverse Events and Serious Adverse Events

An adverse event is defined as any untoward medical occurrence in a subject 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.

The investigators will monitor each subject for clinical and laboratory evidence of adverse events on a routine basis throughout the study. All adverse events will be followed to a satisfactory conclusion.

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.

If an adverse event, whether associated with study drug or not, meets any of the following criteria, it is to be reported to AbbVie clinical pharmacovigilance or contract research organization (CRO) (as appropriate) as a serious adverse event within 24 hours of the site being made aware of the serious adverse event (refer to Section 4.3 of the Operations Manual for reporting details and contact information):

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.

All adverse events reported from the time of study drug administration until 20 weeks (140 days) after discontinuation of study drug administration will be collected, whether solicited or spontaneously reported by the subject. In addition, serious adverse events and protocol-related nonserious adverse events will be collected from the time the subject signs the study-specific informed consent.

AbbVie will be responsible for Suspected Unexpected Serious Adverse Reactions (SUSAR) reporting for the Investigational Medicinal Product (IMP) in accordance with global and local requirements.

Adverse events will be monitored throughout the study to identify any of special interest that may indicate a trend or risk to subjects.

If AEs in any of the following areas of safety interest (ASI) are reported during the study, then the corresponding supplemental report must be completed (Table 3).

Table 3. Adverse Events that Require Supplemental Reports

Adverse Event	Supplemental Report
Cardiac events **Myocardial infarction or unstable angina** **Cerebral vascular accident** **Cardiovascular death**	• Cardiovascular (Cardiac) AE eCRF • Myocardial Infarction and Unstable Angina AE eCRF • Heart Failure AE eCRF • Cerebral Vascular Accident and Transient Ischemic Attack AE eCRF • Combination Thrombotic Event AE eCRF • Arrhythmia AE eCRF
Discontinuation or interruption of study drug due to a hepatic-related AE **Hepatic-related SAE**	Hepatic AE eCRF
Suspected Anaphylaxis Reactions	Hypersensitivity Reaction Signs and Symptoms eCRF
TB Subjects will be screened for TB (using the TB Screening Form) and those with active TB will be excluded from participation in the study. Subjects with events of latent TB or suspected active TB after initiation of study drug should have a TB Supplemental Form completed.	• TB Screening eCRF • TB Supplemental eCRF
Death	Death eCRF

AE = adverse event; eCRF = electronic case report form; SAE = serious adverse event; TB = tuberculosis

Adverse Event Severity and Relationship to Study Drug

AEs must be graded to the 5 criteria as described in the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5,[9] which can be accessed at:

https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf.

If no specific criteria per CTCAE v.5.0 guidelines are available for the reported event, the event should be graded per the investigator's judgment:

- Grade 1 (Mild); asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
- Grade 2 (Moderate); minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living.
- Grade 3 (Severe); medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living.

- Grade 4 (Severe); Life-threatening consequences; urgent intervention indicated.
- Grade 5 (Severe); Death related to AE.

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

Reasonable Possibility	After consideration of factors including timing of the event, biologic plausibility, clinical judgment, and potential alternative causes, there is sufficient evidence (information) to suggest a causal relationship.
No Reasonable Possibility	After consideration of factors including timing of the event, biologic plausibility, clinical judgment, and potential alternative causes, there is insufficient evidence (information) to suggest a causal relationship.

Pregnancy

While not an adverse event, pregnancy in a study subject must be reported to AbbVie within 1 working day after the site becomes aware of the pregnancy. Subjects who become pregnant during the study must be discontinued (Section 5.5). If a pregnancy occurs in a study subject, information regarding the pregnancy and the outcome will be collected.

The pregnancy outcome of an elective or spontaneous abortion, stillbirth or congenital anomaly is considered a SAE and must be reported to AbbVie within 24 hours after the site becomes aware of the event.

6.2 Cardiovascular Adjudication Committee

An independent adjudication committee will be adjudicating all observed cardio- and cerebro-vascular events and will remain blinded to treatment allocation. The events that are adjudicated and the adjudication process will be detailed in the CAC Adjudication Committee Charter. Dedicated eCRFs will be used as outlined in Table 3.

In addition, the site may be contacted for additional source documentation for relevant events.

6.3 Anaphylaxis Adjudication Committee (AAC)

While no concerns with systemic hypersensitivity have been identified with the use of risankizumab, the sponsor has established an independent, blinded, expert committee to adjudicate events of anaphylaxis based on pre-specified definitions. This independent external Anaphylaxis Adjudication Committee (AAC) will adjudicate suspected anaphylactic reactions and will remain blinded to treatment allocation. The event terms to be adjudicated and the adjudication process are detailed in the AAC Charter. A supplemental Hypersensitivity Reactions eCRF will be used to collect information pertinent to the events (Table 3). In addition, the site may be contacted for additional source documentation.

If a suspected systemic hypersensitivity reaction occurs at the investigative site, subjects should be tested for tryptase and histamine levels. If a systemic hypersensitivity reaction such as anaphylaxis is

observed or reported while the subject is not at the investigative site, every effort should be made to obtain tryptase and histamine levels from the treating facility to help better characterize the diagnosis.

6.4 Product Complaint

A product complaint is any complaint 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 (e.g., printing illegible), missing components/product, device not working properly, or packaging issues.

Product complaints concerning the investigational product and/or device must be reported to AbbVie within 1 business day of the study site's knowledge of the event. Product complaints occurring during the study will be followed up to a satisfactory conclusion.

7 STATISTICAL METHODS & DETERMINATION OF SAMPLE SIZE

7.1 Statistical and Analytical Plans

The statistical analysis will be described and fully documented in the Statistical Analysis Plan (SAP). The statistical analyses will be performed using SAS (SAS Institute Inc., Cary, North Carolina, USA).

7.2 Definition for Analysis Populations

The intent-to-treat (ITT) Population, which is defined as all subjects who have at least one dose of study drug in Study M16-005, will be used for the efficacy and usability analyses. The Safety Population, which is defined as all subjects who received at least one dose of study drug in Study M16-005, will be used for all safety analyses. In this study, the safety population is the same as the ITT population.

7.3 Statistical Analyses for Efficacy

All summary statistics for the efficacy analysis will be conducted in the ITT Population. No statistical tests will be performed.

Non-Responder Imputation (NRI) will be used for categorical endpoints. Mixed-effect Model Repeat Measurements (MMRM) will be used for continuous endpoints.

Details on the efficacy analyses are provided in the Statistical Analysis Plan (SAP).

Sample Size Estimation

This study is designed to enroll approximately 100 subjects who will self-administer the risankizumab-AI combination product at Weeks 0, 4, 16, and 28.

Assuming the point estimate is 90% for the proportion of subjects with an observer rating of successful subject self-administration at Week 28, the current sample size of 100 subjects will provide a 95% confidence interval of ± 5.9% around a point estimate.

In addition, assuming comparable response rates as the Phase 3 pivotal studies, with the current sample size of 100, the PASI 90 rate at Week 16 can be estimated with a 95% confidence interval of ± 8.6% when the point estimate is 74%; and the sPGA of clear or almost clear rate at Week 16 can be estimated with a 95% confidence interval of ± 7.0% when the point estimate is 85%.

7.4 Statistical Analyses for Safety

All safety analyses will be performed on the Safety Populations. A treatment-emergent adverse event (TEAE) is defined as an event with onset or worsening after the first dose of study drug and within 20 weeks (140 days) after the last dose of study drug. The number and percentage of subjects experiencing TEAEs will be tabulated using the Medical Dictionary for Regulatory Activities (MedDRA) system organ class (SOC) and preferred term (PT), by severity, and by relationship to the study drug as assessed by the investigator. Summaries (including percentages and events per 100 PYs) of SAEs, deaths, and AEs leading to discontinuation will be provided as well. Pre-treatment AEs will be summarized separately. For selected laboratory parameters, a listing of all subjects with any laboratory value that is above Grade 3 of Common Toxicity Criteria will be provided. Mean change in laboratory and vital signs variables will be summarized. Additional details for the safety analysis are provided in the SAP.

7.5 Study Interim Analysis

An interim analysis will occur after all ongoing subjects complete the Week 28 Visit.

8 ETHICS

8.1 Independent Ethics Committee/Institutional Review Board (IEC/IRB)

The protocol, informed consent form(s), recruitment materials, and all subject materials will be submitted to the IEC/IRB for review and approval. Approval of both the protocol and the informed consent form(s) must be obtained before any subject is enrolled. Any amendment to the protocol will require review and approval by the IEC/IRB before the changes are implemented to the study. In addition, all changes to the consent form(s) will be IEC/IRB approved.

8.2 Ethical Conduct of the Study

The study will be conducted in accordance with the protocol, Operations Manual, International Council for Harmonisation (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 investigator are specified in Appendix B.

8.3 Subject Confidentiality

To protect subjects' confidentiality, all subjects and their associated samples will be assigned numerical study identifiers or "codes." No identifiable information will be provided to AbbVie.

9 SOURCE DOCUMENTS AND CASE REPORT FORM COMPLETION

The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents should be attributable, legible, contemporaneous, original, accurate, and complete to ensure accurate interpretation of data. Clinical site monitoring is conducted to ensure that the rights and well-being of human subjects are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol, ICH Good Clinical Practice (GCP), and applicable local regulatory requirement(s).

10 DATA QUALITY ASSURANCE

AbbVie will ensure that the clinical trial is conducted with a quality management system that will define quality tolerance limits in order to ensure human subject protection and reliability of study results. Data will be generated, documented, and reported in compliance with the protocol, ICH GCP, and applicable regulatory requirements.

11 COMPLETION OF THE STUDY

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

12 REFERENCES

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4. Tsai TF, Blauvelt A, Gong Y, et al. Secukinumab treatment shows no evidence for reactivation of previous or latent TB infection in subjects with psoriasis: a pooled phase 3 safety analysis. J Am Acad Dermatol. 2015;607.

5. Keininger D, Coteur G. Assessment of self-injection experience in patients with rheumatoid arthritis: psychometric validation of the Self-Injection Assessment Questionnaire (SIAQ). Health Qual Life Outcomes. 2011;9:2.
6. Blauvelt A, Prinz JC, Gottlieb AB, et al. FEATURE Study Group. Secukinumab administration by pre-filled syringe: efficacy, safety and usability results from a randomized controlled trial in psoriasis (FEATURE). Br J Dermatol. 2015;172(2):484-93.
7. Nash P, Mease PJ, McInnes IB, et al. FUTURE 3 study group. Efficacy and safety of secukinumab administration by autoinjector in patients with psoriatic arthritis: results from a randomized, placebo-controlled trial (FUTURE 3). Arthritis Res Ther. 2018;20(1):47.
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9. US Dept. of Health and Human Services. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. 27 November 2017. Available from: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf.

APPENDIX A. STUDY SPECIFIC ABBREVIATIONS AND TERMS

AAC	Anaphylaxis Adjudication Committee
AE	Adverse event
AI	autoinjector
ASI	areas of special interest
BCG	Bacille Calmette-Guérin
BSA	body surface area
CAC	Cardiovascular Adjudication Committee
Cardiac	Cardiovascular
CRO	contract research organization
ECG	Electrocardiogram
eCRF	electronic case report form
FSH	follicle-stimulating hormone
GCP	Good clinical practice
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
ICH	International Council for Harmonisation
IEC	Independent ethics committee
IFU	Instructions for Use
IL	interleukin
IMP	Investigational Medicinal Product
IRB	Institutional review board
IRT	interactive response technology
ITT	intent-to-treat
IU	International Unit
IUD	intrauterine device
IUS	Intrauterine hormone-releasing system
mAb	monoclonal antibody
MACE	major adverse cardiac event
MedDRA	Medical Dictionary for Regulatory Activities
MMR	measles-mumps-rubella

MMRM	Model Repeat Measurements
MMRV	measles mumps rubella varicella
NMSC	non-melanoma skin cancer
NRI	non-responder imputation
OPV	Oral polio vaccine
PASI	Psoriasis Area Severity Index
PD visit	Premature Discontinuation visit
PPD	purified protein derivative (tuberculin)
PT	preferred term
SAE	Serious adverse event
SAP	Statistical analysis plan
SC	subcutaneous
SIAQ	Self-injection Assessment Questionnaire
SOC	system organ class
sPGA	static Physician Global Assessment
SUSAR	Suspected unexpected serious adverse reactions
TA MD	Therapeutic Area Medical Director
TB	tuberculosis
TEAE	treatment-emergent adverse event
ULN	upper limit of normal
US	United States

APPENDIX B. RESPONSIBILITIES OF THE INVESTIGATOR

Protocol M16-005: Usability of the Risankizumab Autoinjector Combination Product in Adults with Moderate to Severe Plaque Psoriasis

Protocol Date: 20 March 2019

Clinical research studies sponsored by AbbVie are subject to the International Council for Harmonisation (ICH) Good Clinical Practices (GCP) and local regulations and guidelines governing the study at the site location. In signing the Investigator Agreement, the investigator is agreeing to the following:

1. Conducting the study in accordance with ICH GCP, the applicable regulatory requirements, current protocol and Operations Manual, and making changes to a protocol only after notifying AbbVie and the appropriate Institutional Review Board (IRB)/Independent Ethics Committee (IEC), except when necessary to protect the subject from immediate harm.
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., IEC or IRB) review and approval of the protocol and its amendments.
4. Reporting complaints that occur in the course of the investigation(s) to AbbVie.
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 protocol and all of its 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. Providing direct access to source data documents for study-related monitoring, audits, IEC/IRB review, and regulatory inspection(s).

Signature of Principal Investigator	Date

Name of Principal Investigator (printed or typed)

APPENDIX C. LIST OF PROTOCOL SIGNATORIES

Name	Title	Functional Area
[redacted]	[redacted]	Immunology Development
		Immunology Development
		Clinical Program Development
		Data and Statistical Sciences
		Medical Writing (Protocol Author)

APPENDIX D. ACTIVITY SCHEDULE

The following table shows the required activities across the subject encounters. The individual activities are described in detail in the **Operations Manual**.

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Table 4. Study Activity Schedule

Activity	Screening	Baseline/Week 0	Week 4	Week 16	Week 28	Week 40/PD	Week 48 Follow Up Call
	Day −30 to Day −1	Day 1	Day 28	Day 112	Day 196	Day 280	Day 336
INTERVIEWS & QUESTIONNAIRES							
Informed consent	✓						
Eligibility criteria	✓	✓					
Medical/surgical history	✓	✓					
Demographics	✓						
Alcohol and nicotine use	✓						
Psoriasis and psoriatic arthritis history	✓						
Prior/concomitant therapy	✓	✓	✓	✓	✓	✓	✓
Adverse event assessment	✓	✓	✓	✓	✓	✓	✓
LOCAL LABS & EXAMS							
12-lead ECG	✓						
Physical examination	✓	✓		✓		✓	
Height (screening only) and weight	✓			✓		✓	
Vital signs	✓	✓	✓	✓	✓	✓	
Self-injection assessment (SIAQ) predose		✓					
SIAQ 20 to 40 minutes postdose		✓	✓	✓	✓		

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Activity	Screening	Baseline/Week 0	Week 4	Week 16	Week 28	Week 40/PD	Week 48 Follow Up Call
	Day –30 to Day –1	Day 1	Day 28	Day 112	Day 196	Day 280	Day 336
Observer-rated assessments: - Usability assessment - Use hazard assessments		✓			✓		
Blinded efficacy assessor assessments (PASI, sPGA)	✓	✓	✓	✓	✓	✓	
Blinded efficacy assessor assessment (BSA)	✓	✓					
Local urine pregnancy test (females of child-bearing potential only)		✓	✓	✓	✓	✓	
CENTRAL LABS							
Serum pregnancy/FSH test (females of child-bearing potential only)	✓						
Central total cholesterol, HDL-C, LDL-C, triglycerides		✓				✓	
Central TB screening (local PPD skin test if required)	✓						
Central chemistry and hematology	✓	✓		✓	✓	✓	
Central HIV, Hepatitis B and C	✓						
Urinalysis	✓	✓					
TREATMENT							
Dispense study drug		✓	✓	✓	✓		
Training subject on self-administration		✓					
Subject to self-administer study drug in office		✓			✓		
Collect AI from subject for inspection		✓			✓		

Activity	Screening	Baseline/Week 0	Week 4	Week 16	Week 28	Week 40/PD	Week 48 Follow Up Call
	Day –30 to Day –1	Day 1	Day 28	Day 112	Day 196	Day 280	Day 336
Subject to self-administer study drug at home			✓	✓			

APPENDIX E. PROTOCOL SUMMARY OF CHANGES

Previous Protocol Versions

Protocol	Date
Version 2.0	21 January 2019
Version 1.0	27 November 2018

The purpose of this version is to:

- Clarify required laboratory tests in Appendix D of the protocol
- Add collection of AI from subjects at Week 28 in Appendix D of the protocol
- Clarify study procedures in Sections 4.1, 5.4, and 5.6 of the protocol
- Incorporate AE severity details in Section 6.1 of the protocol
- Update contact information in the Operations Manual
- Clarify study drug administration and follow up-call procedures in Section 2.1 of the Operations Manual
- Clarify clinical laboratory information in Section 3.13 of the Operations Manual
- Clarify drug accountability requirements in Section 5.5 of the Operations Manual
- Correct PASI criteria cut-off percentages in Appendix C of the Operations Manual

APPENDIX F. OPERATIONS MANUAL