Investigator Guidelines and Template	[redacted] VA Health Care System Research Consent Form

VERBAL INTRODUCTION

You are being invited to take part in a research study about an investigational drug called Risankizumab. Before you decide to take part, it is important for you to know why the research is being done and what it will involve. This includes any potential risks to you, as well as any potential benefits you might receive. Taking part in this study is completely voluntary.

Read the information below carefully and discuss it with family and friends if you wish. Ask one of the study staff if there is anything that is not clear or if you would like more details. Take your time to decide. If you do decide to take part in this study, your signature on this consent form will show that you received all the information below, and that you were able to discuss any questions and concerns you had with a member of the study team. If you are participating in any other research study, you must inform the study staff now.

Department of Veterans Affairs

[redacted]

[redacted] VA Health Care System
Research Consent Form

Version Date: 10/30/2019

Principal Investigator / Researcher: [redacted] MD

Title of Study: Clinical Study Protocol M15-991 A Multicenter, Randomized, Double-Blind, Placebo-Controlled Induction Study to Assess the Efficacy and Safety of Risankizumab in Subjects with Moderately to Severely Active Crohn's Disease Who Failed Prior Biologic Treatment (eRD 1191)

1. BRIEF STUDY INFORMATION

A. What is the study about and why are we doing it?

You are being invited to take part in a voluntary research study about the study drug called Risankizumab. The company AbbVie is funding this study. This study hopes to learn how well the medicine Risankizumab works compared to placebo (harmless medicine). If the medicine shows good results, then it can be used for treatment of Crohn's disease.

The drug being tested is experimental, meaning it has not been approved for routine clinical use or for the use described in this study by the United States Food and Drug Administration (USFDA). The USFDA is allowing the use of this drug for research

B. What does the study involve and how long will it last?

The research study can be up to 49 weeks. You will be required to come to clinic and undergo additional testing to make sure the medicine is right for you to take. You may have to come to [redacted] VA Medical Center 4 times before the start of the medicine.

The study drug will be given subcutaneous, meaning under the skin or intravenous (IV), meaning infused into the vein. The infusion will last about 2 hours.

Some of the additional testing that will be done to ensure your safety include: physical exams, urine and blood tests, electrical activity of the heart called an ECG and endoscopies, with or without biopsies. You complete several questionnaires. You will complete a daily diary. an electronic diary. If you are a woman and are or are planning to become pregnant you are not eligible to take part in this study.

C. What are the key reasons I might choose to volunteer for this study?

You may or may not benefit from being in this study but what we learn from your participation may help you or others with Crohn's disease.

D. What re the key reasons I might choose <u>not</u> to volunteer for this study?

You do not have to take part in the study to be treated for your Crohn's disease. Other treatments are available for your Crohn's disease and you may choose not to enroll in the study medicine. You will not be able to participate in the study if you are unable to come to the VA [redacted] hospital for your visits and to receive medicine.

E. Do I have to take part in this study?

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IRB Approval Date: <u>11/13/2019 ajv</u>

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Taking part in this study is completely voluntary. You can choose to participate or not. If you choose not to volunteer in this study, you will not lose any services, benefits, or rights you would normally have.

F. What if I have questions, suggestions, or concerns?

The person in charge of the study is Dr. [redacted] If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study contact [redacted] the study team at extension 5590.

Participant's Name:

_____ _____ _____
Last **First** **Middle**

Last 4: _____

Date of Birth: _____

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RESEARCH DETAILS

2. WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We are asking you to volunteer to take part because you have been diagnosed with moderate to severe Crohn's disease. This study is not to treat you for your Crohn's disease but will compare different doses of the study drug Risankizumab with a placebo. A placebo is a substance that looks like study drug but has no study drug or active ingredient in it, This study hopes to learn how well different doses of the study drug Risankizumab works and the safety of the dosages of study drug compared to placebo to improve the symptoms of moderate to severe Crohn's disease in people who are having symptoms such as diarrhea with or without blood, abdominal pain, and/or sudden and constant feeling that you have to move your bowels. Also, you may have been unable to tolerate or may had insufficient response to treatment with biologic therapies and want to try other options.

This study is being conducted at about 400 research centers worldwide and is expected to enroll a total of 579 participants with moderately to severely active Crohn's disease. The [redacted] VA Health Care System[redacted] will enroll about 10 participants.

3. HOW LONG WILL I BE IN THIS STUDY?

Your total time in this research study could be up to about 49 weeks. This includes a screening period of up to 35 days to determine if you are right to take part, and a 12-week double-blind induction period, at which you will receive study drug. If you receive no response from the first induction period, you may be eligible to take in a second induction period. The second induction period includes about another 3 visits and a 140 day follow up period.

4. WHAT WILL HAPPEN IF I TAKE PART IN THE STUDY?

If you decide to take part in this study, this is what will happen. You will sign this consent form. You will undergo a screening period over about 35 days, to determine if you are right for the study. At the first screening visit you will be given an electronic diary. The electronic diary must be filled in daily for the entire study. This will help the study doctor confirm your eligibility at the beginning of the study and to determine how the drug is working throughout the study. It is important the diary be completed daily.

The study has several periods or phases; a screening period, to determine if you are right for the study. An induction period and a possible second induction period. The induction period is the time from the first time the study drug is given and when a response to the drug is seen. The study phases or periods are described below and in detail in the Study Activities Table that follows.

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If you are enrolled in the study, you will be randomly assigned (by chance, like the flip of a coin) to receive either Risankizumab or placebo (inactive substance that looks like Risankizumab). The placebo is not a drug and it is not expected to have any chemical effects on your body, and it is not designed to treat any disease or illness. This allows the study scientists to make the best judgment on whether the study drug is having effects that are greater than are expected by chance alone.
This is a Double-blind study. Double blind means that neither you nor your study doctor will be able to pick which study drug or dose you receive. However, in case of an emergency, your study doctor can find out this information.

The study drug (Risankizumab) is the active ingredient and is given as a subcutaneous medication (given under the skin) or an intravenous (IV) medication (infused in the vein). The infusion will last about 2 hours.

If you have improved enough during the first 12-week double-blind induction period, you may be eligible to go into the maintenance study for Risankizumab.

If you have not improved enough with the first induction treatment, another 12-week double blind induction period 2, may be started. This period will include about 3-visits to the [redacted] VA and a 140-day follow-up period, from the time of your last dose of study drug medication.

If you do not continue into the maintenance study with Risankizumab, or you end your participation from the study early, you may be asked to come in for additional unscheduled visits, as necessary.

This study was designed to enroll participants for scientific, regulatory and ethical reasons. If the target number of participants has been enrolled, and you are in the screening period, there may be a possibility that you will not be enrolled to complete the study if the targeted number of participants has already been reached.

There are three study groups:

- Group 1 receives 1200 mg of Risankizumab intravenously (through a vein) on study visits Weeks 0, 4 and 8.
- Group 2 receives 600 mg of Risankizumab intravenously on study visits Weeks 0, 4 and 8.
- Group 3 receives placebo intravenously on study visits Weeks 0, 4 and 8.

You will have a 2/3rds chance of receiving Risankizumab for 8 weeks and a 1/3rd chance of receiving placebo for 8 weeks.

Participant's Name:

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Last **First** **Middle**

Last 4: _____

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If after receiving the study induction treatment your Crohn's disease has not improved enough, as determined by your doctor assessment, you will be eligible to receive Risankizumab treatment in an added induction period 2. For this second induction, there are also 3 groups. You will be randomly assigned (by chance, like the flip of a coin) to either groups 1, 2, or 3, if you previously received Risankizumab during the first induction period. For induction period 2, you will receive either Risankizumab infused (intravenous, in the vein) or subcutaneously (injected under the skin); Each group will receive both a placebo and an active treatment. Neither you nor your doctor will know which treatment you are receiving. The induction period 2 is as follows:

- Group 1 in Period 2 receives 1200 mg of Risankizumab intravenously (through a vein) on study visits Weeks 12, 16 and 20. This group receives placebo subcutaneously (under the skin) at Weeks 12 and 20.
- Group 2 in Period 2 receives 360 mg of Risankizumab subcutaneously on study visits Weeks 12 and 20. This group receives placebo intravenously at Weeks 12, 16 and 20.
- Group 3 in Period 2 receives 180 mg of Risankizumab subcutaneously on study visits Weeks 12 and 20. This group receives placebo intravenously at Weeks 12, 16 and 20.

If you received IV placebo during the initial induction treatment you will be assigned, in a double blinded manner, meaning that neither you nor your doctor will know of your assignment, to group 4:

- Group 4 receives 1200 mg of Risankizumab intravenously (through a vein) on study visits Weeks 12, 16 and 20. This group receives placebo subcutaneously (under the skin) at Weeks 12 and 20.

If you have improved enough during the initial 12-week double-blind induction period, you may be eligible to go into the maintenance study for Risankizumab.

If you have not improved enough with the initial induction treatment, an additional 12-week double blind induction period 2, may be started. This period will include about 3-visits to the [redacted] VA Medical Center and a 140-day follow-up period, from the time of your last dose of study drug medication.

Screening Procedures:

During the screening period this is what will happen:

- Informed consent: You will sign and date a study specific IRB approved Informed Consent Form
- Inclusion/Exclusion criteria
- Medical/Surgical History – including questions regarding tobacco, alcohol, and drug use

Participant's Name:

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- Physical Exam
- Vital Signs (blood pressure, heart rate, respiratory rate, and temperature) height and weight
- ECG (a test which records the electrical activity of your heart)
- Endoscopy: During an endoscopy, you will be mildly sedated and a thin, flexible, lighted tube will be inserted inside the bowel. This will allow the doctor to look for abnormal areas. A biopsy might be taken during this test.
- Endoscopic biopsy: An endoscope is a long thin tube with lights that can be passed into the bowel. To perform a biopsy, a small clamp takes a small piece of superficial tissue from an abnormal area seen through the tube.
- Blood and Urine Testing: Blood and urine will be taken to do laboratory tests. For the blood test about 29 ml (6 Teaspoons) will be drawn.
    - Blood and urine tests to monitor your health
    - Blood test for hepatitis B and C - Positive hepatitis test results may be reportable to local public health department according to local laws, if applicable. You may have to sign a separate consent form before hepatitis testing can start.
    - Blood test for HIV: You will not be eligible to take part in this study for study if test results show HIV infection. The study doctor or staff will tell you if the test results are positive. The test is confidential, and the study doctor or staff will not share your results outside of this study unless local law requires it. The results of the test must be negative for you to take part in the study. AbbVie Inc. will not receive results from the testing and will not be made aware of any results, positive or negative).
    - FSH blood test, if you are female and younger than age 55, to determine if you have completed menopause.
- Pregnancy Testing: Test your blood and/or urine to see if you are pregnant. You will only have pregnancy testing if you are a woman and able to become pregnant.
    - The study doctor or study staff will tell you if the pregnancy test results are positive.
    - The results of the pregnancy testing must be negative for you to be in the study.
- Review of any medications you are taking
- PPD Skin Test or QuantiFERON-TB Gold Test (or IGRA equivalent such as T-SPOT) to check for tuberculosis (TB).
- X-ray: There is the possibility that your doctor will request an X-ray, for example, if you have a positive TB test or required by local law.
- Stool samples: you will be required to provide a stool sample for laboratory test.
- Electronic diary: The study site personnel will give you the study electronic diaries and tell you how to use them. You must bring the completed electronic diary back to the study center at each visit.

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Study Visit Procedures:

You will undergo one or more of the study procedures at each study visit:

- Blood Testing: Blood will be taken to do laboratory tests. For the blood about 8.5ml to 11.5ml (1.7 to 2.3 teaspoons) will be drawn at each visit
  - At every visit about 5.5ml (just over 1 teaspoon) of your blood will be taken to test blood cells, chemistry (such as glucose, kidney function and lipids), and to test the degree of inflammation in your body.
  - At certain visits about 3 ml (less than 1 teaspoon) of your blood will be taken to test the amount of Risankizumab in your blood.
  - At certain visits about 3 ml (less than 1 teaspoon) of your blood will be taken to measure the number of certain antibodies in the blood. These are antibodies to the study drug (ADA) and neutralizing antibody (nAb) (antibodies that can block the effects of the study drug) amounts in your blood.
- Vital Signs (blood pressure, heart rate, respiratory rate, and temperature), and weight
- Physical Exam
- Review of any medications you are taking
- Endoscopy at visit Week 12 and also at visit Week 24, if you are in induction period 2. Biopsies may be done when performing the endoscopies.
- Pregnancy Testing: Test your blood and/or urine to see if you are pregnant. You will only have pregnancy testing if you are a woman and can become pregnant
  - The study doctor or study staff will tell you if the pregnancy test results are positive.
  - The results of the pregnancy testing must be negative in order for you to continue in the study.
- Stool samples: you will provide a stool sample for laboratory test
- Urine samples: you will provide a urine samples for laboratory tests.
- Electronic Questionnaires: Instead of using paper and pencil to understand your disease and your response to study drugs, an electronic diary device will be used to collect your answers to questions about your health. This device meets all regulations for use in clinical studies, including those related to your privacy. Your answers to these questions will be transferred to a storage facility via a secure internet connection and will be viewed by site and AbbVie Inc.
- Review Electronic Diary: You should bring the completed electronic diary back to the study center at each visit.
- Study drug administration

Your Responsibilities:

Participant's Name:

_____ _____ _____
Last **First** **Middle**

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For this study to provide useful information about how Risankizumab works, you will be expected to do the following:

- Attend all study visits
- Tell the study doctor if you are feeling bad or worse than before
- Do not change your basic treatment for Crohn's disease before discussing it with they study doctor.
- Tell the study doctor if you have any changes in any medications during the study
- Follow the directions of the study doctor and research team
- Fill out the electronic questionnaires and electronic diary completely and honestly and bring the electronic diary to the study doctor's office at each visit
- Carry your subject card with you as long as you are in the study and show it to any medical staff that may be involved in your healthcare.
- While taking part in this research study, do not take part in any other research project without approval from the study doctor. This is to protect you from possible injury from things such as extra blood drawing, extra X-rays, or possible drug interactions. Taking part in other research studies without first discussing it with the investigators of this study may invalidate the results of this study, as well as that of the other studies.

"A description of this clinical trial will be available on **http://www.ClinicalTrials.gov,** as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

Study Activities Table

	Screening Period (35 Days)	**12-Week Double-Blind Induction**				**Induction Period 2**					
Study Activity	Screening	Baseline (Week 0)	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Premature D/C from Treatment Visit	Unscheduled Visit	140 Day Follow-up[d]
Informed Consent	X										
Inclusion/Exclusion criteria	X	X									

Participant's Name:

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Medical and Surgical History - including questions regarding tobacco, alcohol, and drug use	X	X									
Vital Signs blood pressure, heart rate, respiratory rate and temperature, **Weight and Height**[a]	X	X	X	X	X	X	X	X	X	X	
Physical Exam	X	X	X	X	X	X	X	X	X	X	
ECG (a test which records the electrical activity of your heart)	X										
Endoscopy/Biopsy[b]	X				X			X			
TB Screening	X										
Blood[c] **tests to monitor your health**	X	X	X	X	X	X	X	X	X		
Urine Tests to monitor your health	X	X			X			X	X		
Hepatitis B and Hepatitis C Screening	X										
HIV testing	X										
C. difficile toxin	X										
Blood Test for the assessment of risankizumab (PK) levels in your blood			X	X	X			X	X	X	
Blood Test for the assessment of anti-drug antibody		X	X	X	X			X	X	X	

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(ADA) and Neutralizing Anti-Drug Antibodies (nAb) levels in your blood											
Stool samples		X	X		X			X	X		
Pregnancy Test[e] serum and/or urine (only for females who are able to get pregnant)	X	X	X	X	X	X	X	X	X	X	
Prior and Concomitant Medication Assessment (review of any other medication you are taking)	X	X	X	X	X	X	X	X	X	X	
Adverse Event Assessment (review of any side effects you are experiencing, which may or may not be related to the study drug)	SAEs only	X	X	X	X	X	X	X	X	X	X
Dispense Subject Diary	X										
Patient Questionnaires: CSS		X	X	X	X	X	X	X	X	X	
Patient Questionnaires: PGIC			X	X	X	X	X	X	X	X	
Subject Questionnaires: EQ-5D-5L FACIT-F IBDQ		X	X		X			X	X		

Participant's Name:

_____ _____ _____
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SF-36 WPAI-CD											
Study Drugs Dispensing/ Administration[f]		X	X	X	X	X	X				
Daily diary review		X	X	X	X	X	X	X	X	X	

D/C = Discontinuation Please note that you may be asked to repeat a procedure or test if your study doctor feels it is needed to evaluate your condition.

a. Height will be measured at Screening only.
b. You will undergo a full colonoscopy with biopsy during Screening and Week 12 visit. If you enter induction period 2, you will undergo an additional endoscopy at Week 24.
c. For some of the blood samples it is preferable to be collected while patients are in fasting condition.
d. You will be contacted 105 days following study drug discontinuation for an assessment of any new or ongoing adverse events, except those subjects who will roll over into risankizumab maintenance study M16-000. During this follow-up call the results of the follow-up at home pregnancy test should be communicated to the site by you.
e. A serum pregnancy test will be performed on all women of childbearing potential at Screening. Urine pregnancy test will be performed at the site at Baseline all subsequent visits for all women of child bearing potential. If any urine pregnancy test is positive, a serum pregnancy test will be performed at the site and sent to the central laboratory. If a pregnancy is identified, the pregnancy must be reported to AbbVie
f. Study drug will be administered intravenously (through a vein) during your site visits at Baseline, Week 4, and Week 8, after all assessments and examinations scheduled for that day have been completed. Study drug will only be administered at week 12 if you enter induction period 2. Study drug administration at week 12 will be intravenous and subcutaneous (under the skin)

5. WHAT POSSIBLE RISKS OR DISCOMFORTS MIGHT I HAVE IF I TAKE PART IN THIS STUDY?

There is always a chance that any procedure can harm you. The procedures in this study are no different. In addition to the risks described above, you may experience a previously unknown risk or side effect. Risks of the usual care you receive are not risks of this study. Those risks are not included in this consent form. You should talk with your health care providers if you have any questions about the risks of usual care.

Possible risks of the Study:

- Questionnaires**:** Some people become uncomfortable at being asked questions about their medical condition; if, for any reason, you wish not to answer specific questions, or you wish to terminate the session, you will be able to do so.

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_____ _____ _____
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- Photographs: There will be no photographs, audio tapes, or video tapes made of you as part of this study. The only video taken for this study is the video capture by the endoscopic camera, if needed during the endoscopic procedure to document the condition of the bowel. You will not be identified personally.
- Confidentiality: Even though the risk is small, it is possible that your data could be seen by someone who does not have permission to see it.
- Blood Draw: There may be some discomfort, bruising, or bleeding at the site where the blood is drawn. Sometimes people faint from a blood draw.
- Electrocardiogram (ECG): There is no pain or discomfort during an ECG; however, removing the pads may cause some irritation to your skin.
- Physical Exam: There are no special risks with an exam, similar to examinations you have had in your doctor's office in the past.
- Intravenous (IV) infusion of study drug: a thin needle is placed inside the vein and could cause similar risks to the ones described in the blood draw.
- Subcutaneous Injection of study drug: a needle is used to inject the study drug or placebo under the skin. This can cause skin irritation and/or itching.
- Placebo: a placebo is not designed to have any chemical effects on your body. No risks are expected from a placebo.
- PPD test (to test for TB infection): there may be slight discomfort where injection is administered. Rarely people can have a larger skin reaction at the site. This may require treatment for a couple of days.
- Serum Pregnancy Testing: The risks are similar with any blood test.
- QuantiFERON test or T-SPOT TB (to test for TB infection): The risks are similar to any blood tests.
- X-ray. You may have an X-Ray to check your lungs for TB infection: There can be risks of radiation from the X-ray. The total amount of radiation exposure that you will receive is about 0.02 mSv or 2 mrem. It is about the same amount of radiation exposure of 2 days of exposure to natural background radiation. The radiation involved is minimal risk. You may ask the study doctor or study staff if you have questions about the risks of the study procedures.
- Endoscopy/ Biopsy: endoscopies may be either a full colonoscopy or a flexible sigmoidoscopy. A colonoscopy, sigmoidoscopy and biopsy of the colon are standard and commonly performed medical procedures to examine the large bowel. This procedure may involve some pain and discomfort. Rare complications include tearing of the colon and/or bleeding that may require surgical repair. When a biopsy (removal of a small piece of tissue) is performed during the colonoscopy, bleeding from the biopsy site may occur. Other complications that may occur include infection at the biopsy site and bacteria in the blood. If sedation is to be given for the

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procedure, your study doctor will discuss with you the risks of sedation. You will not be permitted to drive immediately after the procedure and, therefore, will need someone to drive you home. You will be asked to sign a separate consent for the colonoscopy. Additional risks for the procedure include the rare occurrence of bowel perforation (creation of a hole in the bowel) and/or bleeding which might require surgery and/or the use of antibiotics. Following the removal of tissue for biopsy, you may see a small amount of blood in your stools.

- Fasting for up to 8 hours could cause dizziness, headache, stomach discomfort, or fainting.

Study Drug Risks; Risankizumab Risks
No adverse effects were seen in animals given Risankizumab up to 26 weeks.

Risankizumab has been given to healthy volunteers and patients with psoriasis, psoriatic arthritis, inflammatory bowel disease, ankylosing spondylitis, and asthma. Risankizumab has been given either by intravenous infusion (IV, slowly injected into a vein in the arm) or by subcutaneous injection (injection into the deepest skin layer).

Taking the study drug in this study may cause you to have one or more of the side effects (or adverse events) as listed below.

In a Phase II psoriasis study, 126 patients received Risankizumab by subcutaneous injection (injected into the deepest skin layer). The most commonly reported side effects were nasopharyngitis (inflammation of the nasal passage, 32%), headache (9%), back pain (6%) and arthralgia (joint pain, 5%). In general, there was no difference in rates of the side effects between patients who received Risankizumab and those who received an approved drug for psoriasis or psoriatic arthritis (ustekinumab) and no evidence that the events were related to the dose of Risankizumab. There were eleven (9%) Risankizumab patients with serious side effects as compared to three (8%) patients with serious side effects in 40 patients receiving Ustekinumab. All serious side effects were considered not related to Risankizumab by the study doctor, except one case of basal cell carcinoma (a type of skin cancer).

Eighty-two patients received Risankizumab in a Crohn's disease (inflammatory bowel disease) ongoing blinded Phase II study. The most commonly reported side effects in the Risankizumab treatment groups were: nausea (13% of subjects), arthralgia (joint pain, 15%), headache (12%), abdominal pain (11%), vomiting (6%), asthenia (lack of energy, 6%), diarrhea (5%) and pyrexia (fever, 5%). The rates were similar to the placebo group except the rates of arthralgia (8%) and asthenia (5%) were lower in the placebo group. The rates of serious side effects were lower in the Risankizumab treatment group compared to the placebo treatment group (15% vs 31%).

Other Potential Risks

Other monoclonal antibodies that affect the immune response have been associated with side effects such as increased risk of infection, serious allergic reactions, injection site reactions (if given subcutaneously), and possible increased risk of malignancy (cancer). These side effects have not been found associated with Risankizumab.

Infections: Drugs that affect the body's immune system may increase the risk of infections, including tuberculosis. There is insufficient information now to know if treatment with Risankizumab will lead to an increased risk of infections. You will be screened for signs of active infection before you start on Risankizumab.

Allergic Reactions: All drugs have a potential risk of an allergic reaction. Allergic reactions may vary from mild (rash, hives, itching) to severe reactions such as anaphylaxis (which may include difficulty breathing, swelling of the face or throat, low blood pressure, or loss of consciousness). A severe allergic reaction requires immediate medical treatment and could result in permanent disability or death. It is important to tell your study doctor about any past allergic reactions that you may have had to other drugs including antibody drugs (which are usually given by IV or injection under the skin).

Injection Site Reactions: Injection of study drug under the skin could result in redness, pain, swelling or hardness at the site of the injection. Also bleeding or bruising at the injection site may occur. Most injection site reactions are not severe and resolve without any treatment but can be uncomfortable for a few hours to a few days.

Infusion Site Reaction: Giving study drug by IV may result in an infusion-related reaction with symptoms such as fever, flushing of skin, itching, rash or a decrease in blood pressure. If you are receiving study drug IV your doctor will monitor for signs of adverse reaction during the infusion.

Malignancy (cancer): When an immune system pathway is blocked, there is a possibility of a decreased immune defense against malignancies. In the completed studies to date, Risankizumab has not been associated with an increased risk of malignancies but the risk with long term therapy is not known.

Cardiovascular Events: In addition, an increased risk of major cardiovascular events (such as heart attacks, strokes or cardiovascular death) have been reported in patients with moderate to severe psoriasis and psoriatic arthritis. Whether receiving Risankizumab further increases the risk of major cardiovascular events is unknown. Any new or worsening signs or symptoms such as chest, neck or

arm pain, shortness of breath, sensation of rapid heart rate, new visual symptoms or muscle weakness should be immediately reported to your study site and/or primary health care provider.

An antidote against Risankizumab is currently not available. Any side effects occurring because of Risankizumab will be treated symptomatically.

Pregnancy risks, risk to nursing infant and contraceptive precautions
The safe use of Risankizumab in pregnant women and nursing mothers has not been established. Consequently, there may be risks to you (or to your embryo or fetus) if you are or may become pregnant that are unknown. Women of childbearing potential enrolling in this study must have a negative pregnancy test and must agree to continue to use a birth control measures for the duration of the study. If, while participating in the study, you suspect you have become pregnant, please contact the study physician immediately. Nursing mothers may not take part in this study.

If you are a woman who can have children, the study doctor or study staff will talk to you about birth control you must use during study participation and 16 weeks after your last dose of study drug. If you are able to become pregnant, you must agree to use at least one accepted method of contraception during the study including up to 16 weeks after last dose of study drug.

Acceptable methods of contraception in this study are:

- Combined (estrogen and progestogen containing) hormonal birth control (oral, intravaginal, transdermal) associated with inhibition of ovulation
- Progestogen-only hormonal birth control (oral, injectable, transdermal) associated with inhibition of ovulation
- Bilateral tubal occlusion/ligation
- Intrauterine device (IUD)
- Intrauterine hormone-releasing system (IUS)
- Male or female condom with or without spermicide
- Cap, diaphragm, or sponge with spermicide
- 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).

Some methods of birth control will not work when you are taking certain drugs. If you decide to take part in this study and you are able to become pregnant, a pregnancy test will be done before your

participation in the study and at other visits if necessary.

You also may take part in this study if you are surgically sterilized (both ovaries or fallopian tubes removed or uterus removed) or you are post-menopausal (no menses for at least 1 year without other cause identified).

Once you're enrolled in the study, if you become pregnant or think you could be pregnant, it is important for you to tell the study doctor or staff immediately. If you become pregnant during the study, you will no longer receive study drug. Even if you are no longer in the study or not receiving study drug, your study doctor will contact you about the outcome of the pregnancy including following the birth of an infant to find out about the baby´s health. Outcomes collected will include the fetal number and fetal outcome, date of delivery, birth weight and length, sex, any medically significant complications with the mother and/or baby and the presence of any birth defects.

Unknown Risks
You may experience side effects that are not listed in this informed consent. As with any investigational drug, administration of Risankizumab may involve risks that are currently unknown, including life threatening reactions or the remote possibility of death.

You should notify the study doctor of any changes in your health or new symptoms you are experiencing, even if you think these changes are not related to study drug.

You will be told of important new information about this study or the study drug that becomes available and that may affect your willingness to take part in this study.

Safety Monitoring:
Blood test, vital signs, ECG, and physical exams will be done through-out the study.

Tell your doctor if you develop any signs of infection including fever, sweats, chills, flu-like symptoms, cough shortness of breath, feeling tired, diarrhea, skin rashes or sores, burning when you urinate or urinating more often than normal.

6. WHAT ARE THE POSSIBLE BENEFITS OF THIS STUDY?

You may or may not benefit from being in this study, but knowledge gained from your participation in this research study may benefit future patients with Crohn's disease.

7. WHAT OTHER CHOICES DO I HAVE IF I DO NOT WANT TO JOIN THIS STUDY?

Department of Veterans Affairs

[redacted]

[redacted] VA Health Care System
Research Consent Form

Version Date: 10/30/2019

Principal Investigator / Researcher: [redacted] MD

Title of Study: Clinical Study Protocol M15-991 A Multicenter, Randomized, Double-Blind, Placebo-Controlled Induction Study to Assess the Efficacy and Safety of Risankizumab in Subjects with Moderately to Severely Active Crohn's Disease Who Failed Prior Biologic Treatment (eRD 1191)

You do not have to take part in this study to be treated for your Crohn's disease. Other treatment options for your Crohn's disease are available. Other treatment choices may include getting standard of care for Crohn's disease without being in the study or taking part in another study. You may discuss these options with your doctor

8. HOW WILL MY PRIVATE INFORMATION BE PROTECTED?

The VHA complies with the requirements of the Health Insurance Portability and Accountability Act (HIPAA) of 1996 and its privacy regulations and all other applicable laws that protect your privacy as a VA patient. Individually identifiable data collected from you will be stored at [redacted] VA under lock and key in the study team office; on password-protected VA computer systems accessible only to the study team. Your records will have a unique code in place of information that can be used to identify you (such as your name or address). The sponsor and companies working with the sponsor will have access to coded records and accompanying data to conduct the research. However, they will not be able to see the key that links the code to you. We will include information about your study participation in your medical record.

There are times when we might have to show your records to other people for monitoring and auditing purposes. For example, someone from the Office of Human Research Protections, the Government Accountability Office, the Office of the Inspector General, the VA Office of Research Oversight, the Institutional Review Board, our local Research and Development Committee, the FDA and other study monitors may look at or copy portions of records that identify you.

Data that can be individually identified as yours will be shared outside of [redacted] VA with only the study sponsor and its safety oversight committee (AbbVie, 1 North Waukegan Road, North Chicago, IL 60064); the laboratory that performs the tests on your samples ([redacted]); the imaging center [redacted]; contractor for the proper collection of data [redacted] and diary entries [redacted]

Despite these protections, once your information is shared outside of [redacted] VA, there is a possibility that your information may no longer be protected by Federal laws or regulations and may be subject to re-disclosure by the recipient.

All other data shared outside of the study team will be released in a way that you cannot be individually identified. Information about you will be combined with information from other people taking part in the study. We will write about the combined data we have gathered. Any talks or papers about this study will not identify you.

Participant's Name:

_____ _____ _____
Last **First** **Middle**

Last 4: _____

Date of Birth: _____

[redacted] **IRB USE ONLY**

IRB Approval Date: 11/13/2019 ajv

Form valid only if the above completed.

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Department of Veterans Affairs

[redacted]

[redacted] VA Health Care System
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Principal Investigator / Researcher: [redacted] MD

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A more detailed description of how we will use and protect your private information will be provided to you in a separate document, known as a HIPAA Authorization.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

9. WHAT WILL HAPPEN IF I AM INJURED BECAUSE OF MY BEING IN THE STUDY?

Every reasonable safety measure will be used to protect your well-being. If you are injured because of taking part in this study, the VA will provide necessary medical treatment at no cost to you unless the injury was due to your not following the study procedures. You do not give up any of your legal rights and you do not release the VA from any liability by signing this form.

If you should have a medical concern or get hurt or sick as a result of taking part in this study, call the study investigator Dr. [redacted] during the day at [redacted]. If after hours, contact [redacted] VA Health Care System operator at [redacted] by pressing 0 or by staying on the line until they answer. You should inform the operator that you are in a research study and give the name of the Principal Investigator of this study.

For emergency care, you should call 911 or VA Emergency Department [redacted] If any medical problems occur in connection with this study, the VA will provide emergency care. You can also contact your Primary Care Provider in case you have any additional medical problems or questions. Emergency and ongoing medical treatment will be provided as needed.

The next statement is the policy of the outside sponsor of this study and does not waive any of your rights as a Veteran or as a research subject, or your rights to legal recourse:

> Treatment for injuries that results from the study drug or study procedures is available. Your study doctor will discuss with you the available medical treatment options. You may arrange to have treatment performed by the study doctor or a licensed doctor selected by you.
>
> AbbVie Inc. makes no commitment to provide compensation except as described above.

10. PERSONS TO CONTACT ABOUT THIS STUDY

If you have questions or concerns about the study, please contact the study investigator Dr. [redacted] or the study team [redacted].

Participant's Name:

_____ _____ _____
Last **First** **Middle**

Last 4: _____

Date of Birth: _____

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[redacted]

[redacted] VA Health Care System
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Version Date: 10/30/2019

Principal Investigator / Researcher: [redacted] MD

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If you have any questions about the conduct of this study or about your rights as a participant in this study, you should contact the Research Service Champion, [redacted] The Champion will follow-up and may further connect you, as appropriate, with the Chairperson of the Institutional Review Board (IRB), the Chairperson of the Research and Development Committee, the Research Administrative Officer, or the Research Compliance Officer.

11. PARTICIPATION IS VOLUNTARY

It is up to you to decide whether to take part in this study or not. If you decide to take part, you may still withdraw at any time. To withdraw your consent to participate, you need to inform the investigator or study team. Once you have withdrawn your consent, no further study visits are required

However, if you decide to end your participation early, you may be asked to return for a last visit as soon as possible to check on your health. You may also have a follow-up call 140 days from the last dose of the study drug to find out how you are doing. If you withdraw in writing your participation in the study ends.

If you do not wish to be in this study or leave the study early, you will not lose any benefits to which you are entitled. If you do not take part, you can still receive all usual care that is available to you. Your decision not to take part will not affect the relationship you have with your doctor or other staff, and it will not affect the usual care that you receive as a patient.

Data already collected for the study prior to your withdrawal, may continue to be reviewed by the study investigator but no further information will be collected, except from public records, such as survival data. Any specimens already used cannot be withdrawn.

The HIPAA Authorization which permits VA to use and release your medical record is a separate form that, unlike this consent form, must be revoked in writing. To ensure that VA cannot be forced to access your health records for this study after you withdraw your consent, you should also revoke your HIPAA Authorization. The study team can provide a HIPAA revocation form for you to use, or you can send a written statement that you revoke your HIPAA authorization to the revocation address on the study's HIPAA Authorization form.

12. RIGHT OF INVESTIGATOR TO TERMINATE MY PARTICIPATION

At any time, your study doctor may stop your participation for any reason regardless if you signed consent. The study doctor may decide to stop your participation without your permission if they think that being in the study may cause you harm or for any reason. The study sponsor AbbVie may stop the study prematurely for any reason, either in its entirely or at any site

Participant's Name:

_____ _____ _____
Last **First** **Middle**

Last 4: _____

Date of Birth: _____

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13. WHAT IS THE COST TO ME AND PAYMENT FOR ME IF I TAKE PART IN THIS STUDY?

A. Costs to Participants:

You will not be charged for any treatments or procedures that are part of this study. If you usually pay co-payments for VA care and medications, you will still pay these co-payments for VA care and medications that are not part of this study.

B. Payment Offered for Participation:

You will not be compensated for your time and effort taking part in this study.

However, you will receive $50.00 per visit. The total amount possible for study participation is $400.00.

The stipend will be on a ClinCard, which works like a gift/credit card. When visits are completed, funds will be loaded onto your card. You will be able to use the funds in approximately one business day. If you have issues when using this ClinCard, please contact the study team. The provider of the ClinCard (Greenphire) will not have access to your name or contact information. Instead, they will have your study ID number that will be provided to you by the study coordinator. You will be able to use this study ID number to check the balance on your ClinCard. If your ClinCard is lost or stolen, Greenphire cannot cancel your card if is lost or stolen, and the entire current balance on the card may be lost. However, you will be issued a new card for future payments. If you get more than $600 in one year from ClinCard, this will generate Internal Revenue Service (IRS) form 1099. Your SSN will be used for this purpose.

14. WILL I BE TOLD NEW INFORMATION ABOUT THIS STUDY?

During the course of a research study, if new information becomes available about Risankizumab that might change a person's decision to stay in the study, your research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw from the study, your research doctor will arrange for your medical care to continue. If you decide to continue in the study, you might be asked to sign an updated informed consent form. Your research doctor could also decide to withdraw you from the study in your best interests. If so, he or she will explain the reasons and arrange for your usual medical care to continue.

Tests done for research purposes are not meant to provide information for clinical treatment. Your individual results for this study will not be provided to you. There is a slight possibility that during this study, an investigator could discover something that could affect the health of you or your family. If this occurs, the finding will be reviewed by the study team to determine if it is in your best interest to contact you. If so the investigator will contact you using the information you provided. With the help of an appropriate medical specialist, they will present possible risks or benefits of receiving the information. At that time, you can choose to receive or refuse to receive the result or finding.

Participant's Name:

_____ _____ _____
Last **First** **Middle**

Last 4: _____

Date of Birth: _____

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15. WHO COULD PROFIT FROM THE STUDY RESULTS?

The use of your donated sample may be used for research that may result in scientific discoveries that may lead to new products, tests, or treatments. These discoveries may have potential commercial value. If this occurs, there are no plans to provide financial payment or benefits to you or your relatives.

Participant's Name:

_____ _____ _____
Last **First** **Middle**

Last 4: _____

Date of Birth: _____

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AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY

The Principal Investigator [redacted] or his/her study team has explained the study to me. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other alternatives available to me. I have been given the chance to ask questions and obtain answers. I will receive a copy of this consent.

By signing this document below, I voluntarily consent to participate in this study. I also confirm that I have read this consent, or it has been read to me. A copy of this signed consent will also be put in your medical record.

I agree to participate in this research study as has been explained in this document.		
_____ Participant's Name	_____ Participant's Signature	_____ Date
_____ Name of person obtaining consent	_____ Signature of person obtaining consent	_____ Date

Participant's Name:

_____ _____ _____
Last **First** **Middle**

Last 4: _____

Date of Birth: _____

[redacted] **IRB USE ONLY**

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