Research Subject Information and Consent Form – 25 February 2016

Study Title:	A Phase 4 Trial Assessing the ImPact of Residual Inflammation Detected via Imaging TEchniques, of Drug Levels and Patient Characteristics on the Outcome of Dose TaperIng of Adalimumab in Clinical Remission Rheumatoid ArThritis (RA) subjects (PREDICTRA)	
Protocol Number:	M14-500	
Sponsor:	For Non-EU Countries: AbbVie 1 North Waukegan Road Bldg. AP31-3 North Chicago, IL 60064 USA	For EU Countries: AbbVie Deutschland GmbH & Co. KG (AbbVie) Knollstrasse 50 67061 Ludwigshafen Germany
Study Doctor:	**[Insert investigator's name]**	
Telephone:	**[Insert site's contact numbers]**	
After Hours:	**[Insert site's after hours contact numbers, if applicable]**	

Before you can make an informed decision to participate in this research study, you should understand the possible risks and benefits of this study. This process is known as informed consent. **[Insert proper EC term here]** has approved the information in this consent and has given approval for the study doctor to conduct the study. An Institutional Review Board (IRB)/Ethics Committee (EC) is an independent committee made up of a group of independent experts and lay persons set up to help protect the rights of research subjects. This does not mean the IRB/EC has approved your participation in the study. It also does not mean the study is without risk. This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family, friends or anyone you choose before making your decision. If you decide to participate in this study, you will be asked to read and sign this consent form to confirm that you have had the study explained to

you, and you have agreed to participate. You will receive a copy of the signed consent form.

When reading this form, please note that the words "you" and "your" refer to the person in the study rather than to a parent/guardian or legally authorized representative who might sign this form on behalf of the person in the study.

[For EU sites] Please insert a statement that positive opinion of Ethics Committee has been obtained.

Introduction

You have been asked to participate in a research study of a drug called Humira®, adalimumab. Adalimumab has been approved by the regulatory authorities in your country, and in other countries, including the United States (US), Food and Drug Administration (FDA) and the European Medicines Agency to treat rheumatoid arthritis in a recommended dose of 40 mg given by subcutaneous injection every two weeks. Therefore, the use of adalimumab 40 mg every three weeks or its withdrawal is investigational (experimental) for the purposes of this study. AbbVie is sponsoring this study. AbbVie is paying the study doctor to perform this study.

You have been asked to participate in this trial because you have rheumatoid arthritis (RA), and you are being treated with adalimumab 40 mg every other week combined with a methotrexate or another conventional synthetic disease-modifying anti-rheumatic drugs (csDMARD) at a dose recommended by your physician and your disease is under control and considered in clinical remission for the past 6 months. There is a limit of 20% enrolled subjects in the study on other csDMARDs or no csDMARDs. Once this limit is met, only subjects on concomitant methotrexate will be allowed into the trial. You are experiencing little to no signs and symptoms of rheumatoid arthritis.

While the majority of research studies have been conducted to demonstrate the efficacy and safety of the use of adalimumab every other week for the treatment of rheumatoid

arthritis, this study will be evaluating characteristics of the disease and subjects who can reduce the dose of adalimumab to 40 mg every three weeks.

Being in this study does not replace your regular medical care.

Purpose of the Study

The purpose of this study to investigate the association between subject's characteristics, including residual joint inflammation and the risk of RA flare after reducing the dose or withdrawing adalimumab. This could help physicians identify which subjects might be able to reduce their adalimumab dose without losing clinical remission.

Study Information

This multinational study is expected to be conducted at approximately 72 research centers in the European Union, Australia, United States and Canada. Approximately 200 subjects with RA will participate in this study.

This study was designed to enroll 200 subjects for scientific and ethical reasons; therefore, if the target number of subjects has been enrolled, and you are in screening, there is a possibility that you will not be enrolled.

Your participation in this study will last approximately 40 weeks or as long as 56 weeks if you experience a flare and includes up to 12 study visits (not including unscheduled visits) to the research center.

There will be an initial Screening Period, which can last up to 28 days. The Screening Period will be followed by a Lead-In Period of 4 weeks during which everyone will receive adalimumab 40 mg every other week. Your study doctor will determine whether you are able to enter the study based on evaluations at the Screening and at the Lead-In Week 0 visits.

After the Lead-In Period, you will come to the office for a Week 4 (Double-Blind Baseline) Visit. If it is confirmed that you are considered in clinical remission (your

disease is under control), you will be randomly assigned by chance to receive either adalimumab every three weeks or placebo (inactive substance) that looks like adalimumab every three weeks. You will have an 83% chance (5 in 6) of receiving adalimumab and a 17% chance (1 in 6) of receiving placebo. Neither you nor your study doctor or study staff will be able to pick which study drug you'll receive. This is a double-blinded study, which means neither you nor your study doctor or study staff will know to which study treatment you were assigned. In case of an emergency, your study doctor will be able to find out this information, if he or she feels it is necessary in order to treat you.

The Double-Blind period which starts at Week 4 (called Double-Blind Baseline Visit) will last approximately 36 weeks: you'll have study visits every 6 weeks: at Weeks 10, 16, 22, 28, 34 and 40 or if you discontinue early from study.

If at any time you think you have a flare, you should call your study doctor to schedule a visit (if you don't already have your normally scheduled visit within the next 2 weeks). At this visit, your study doctor will investigate if your experience is a rheumatoid arthritis flare. If a flare is confirmed during the Double-Blind period, you will enter into the Open-Label Rescue Arm which consist of stopping the double-blinded study drug and initiating adalimumab 40 mg every other week starting at Flare Week 0 and up to 16 weeks. If it is determined you do not have a flare, you will continue in the study at your regular scheduled visits.

During the Open-Label Rescue Arm, you will have 4 Visits (Flare Week 0, Flare Week 4, Flare Week 10 and Flare Week 16); your study doctor will discuss with you and decide which medications can be added to your regimen of adalimumab every other week to control your flare.

Adalimumab will be provided in a pre-filled syringe for injection under the skin (subcutaneous). If needed, the study staff will review with you (or someone who can do it for you) how to give yourself these injections. If you are unable to receive these injections, you should not enter this study.

To be in this study, you must agree not to take concomitantly any of the following treatments: other than the study biologic therapy (examples are etanercept, infliximab, golimumab, certolizumab and tocilizumab), live vaccines (during the study and for 70 days after the last dose of study drug), the combination of Rifampin/Pyrazinamide, anti-retroviral therapy, not allowed conventional synthetic Disease Modifying Anti-Rheumatic Drugs (csDMARDs) (e.g., azathioprine, cyclophosphamide, d-penicilamine), opioid analgesics (other than tramadol or similar) or marijuana and any drug that is considered investigational.

You must agree to stay on the same dose of some of the medications you are taking, including but not limited to methotrexate. Your study doctor will explain in detail which medications you can or cannot take.

During the study, you must ask your study doctor before changing or taking any new medicines, including herbal medicines, or non-prescription medicines you buy at a grocery store or drug store. Ask your study doctor before you get any vaccinations during this study. If you started on TB preventative medicine prior to entering the study or any time during the study, you must continue the TB medicine for the full duration prescribed or as instructed by your study doctor.

Procedures

Study Procedures

If you agree to be in this study, you will undergo some activities, tests and evaluations to determine if you are eligible for this study. Such tests and evaluations are completed during a Screening Period that takes place before participation in the main part of the study. If you are eligible to participate in this study, you will undergo the procedures listed in the table below.

Table 1. Activities and Procedures

Activity*	SCR (28 days)	Lead-In Period (Wk 0)	Randomized Double-Blind Period							Open-Label Rescue Arm				ET	UV
			Week							Flare Week					
			Double-Blind Baseline (Wk 4)	10	16	22	28	34	40	0	4	10	16		
Medical History – including questions regarding tobacco and alcohol use at Screening	X	X													
Physical Exam and Vital Signs (blood pressure, heart rate, respiratory rate and temperature), including height and weight	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Rheumatoid arthritis evaluation(your study doctor will assess severity of your rheumatoid arthritis)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Complete questionnaires on the severity of your disease, general functioning and well being	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Ultrasound, a non-radiation ecographic evaluation of damage to several of your joints which might be affected by RA **(remove if site is not participating in Ultrasound portion)**			X							X					
Electrocardiogram (an harmless test which records the electrical activity of your heart)**	X														

Table 1. Activities and Procedures (Continued)

Activity*	SCR (28 days)	Lead-In Period (Wk 0)	Randomized Double-Blind Period							Open-Label Rescue Arm				ET	UV
			Week							Flare Week					
			Double-Blind Baseline (Wk 4)	10	16	22	28	34	40	0	4	10	16		
Chest x-ray (a 'picture' that shows clinically relevant findings)**	X														
Magnetic Resonance Imaging (MRI) a test to evaluate the 3-dimensional structure and damage of your hand and wrist		X							X				X	X	
Tuberculosis Testing (to determine if you have been exposed to tuberculosis (TB infection)***	X														
Hepatitis B Virus Test (approximately 3.5 mL [approximately < 1 tsp] of blood).**	X														
Serum Pregnancy Test (approximately 1.0 mL [approximately < 0.5 teaspoon (tsp) of blood] for women who are able to have children)	X														
Urine Pregnancy Test (approximately 2.0 mL [approximately < 0.5 teaspoon (tsp) of urine] for women who are able to have children)		X							X				X	X	

Table 1. Activities and Procedures (Continued)

Activity*	SCR (28 days)	Lead-In Period (Wk 0)	Randomized Double-Blind Period							Open-Label Rescue Arm				ET	UV
			Week							Flare Week					
			Double-Blind Baseline (Wk 4)	10	16	22	28	34	40	0	4	10	16		
Blood tests related with RA inflammation (approximately 3.7 mL approximately < 1.0 teaspoon [tsp] of blood)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Routine Blood Tests (approximately 7 mL per visit [approximately < 1.5 tsp] of blood) to check on your overall health and disease state	X	X		X	X		X		X	X		X	X	X	
Blood drawn to help identify characteristics of rheumatoid arthritis (also called Biomarker Sampling) (approximately 6 mL per visit [approximately 1.2 tsps] of blood).			X	X	X		X		X	X	X		X	X	
Optional biomarker samples for future research (approximately 6 mL per visit [approximately 1.2 tsps] of blood). Sample will be drawn only if consent is obtained.			X	X	X		X		X	X	X		X	X	

Table 1. Activities and Procedures (Continued)

Activity*	SCR (28 days)	Lead-In Period (Wk 0)	Randomized Double-Blind Period							Open-Label Rescue Arm				ET	UV
			Week							Flare Week					
			Double-Blind Baseline (Wk 4)	10	16	22	28	34	40	0	4	10	16		
Optional blood drawn to look at pharmacogenetics related with RA – DNA (approximately 3 mL [approximately half a tsp] of blood). Sample will be drawn only if consent is obtained.			X						X				X	X	
Optional blood drawn to look at pharmacogenetics related with RA (mRNA) (approximately 5 mL [approximately 1 tsp] of blood). Sample will be drawn only if consent is obtained.			X	X	X		X		X	X	X		X	X	
Blood drawn to measure how much study drug is in your blood and to develop future measurements (approximately 2 mL per visit [less than half a tsp] of blood)			X	X	X		X		X	X	X	X	X	X	

Table 1. Activities and Procedures (Continued)

Activity*	SCR (28 days)	Lead-In Period (Wk 0)	Randomized Double-Blind Period							Open-Label Rescue Arm					
			Week							Flare Week					
			Double-Blind Baseline (Wk 4)	10	16	22	28	34	40	0	4	10	16	ET	UV
Blood drawn to measure whether or not you have built up antibodies to the study drug and to develop future measurements (approximately 2 mL per visit [less than half a tsp] of blood)			X	X	X		X		X	X	X	X	X	X	
Urine Test	X		X		X		X		X	X			X	X	

Early Termination = ET; Week = Wk; Unscheduled Visit = UV

* 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.

** Unless you have had one within 12 months, the results are available to the site study staff and there has been no significant change in your circumstances that calls for a repeat of the assessment.

*** Unless you have had one within 12 months, the results are available to the site study staff and there has been no significant change in your circumstances that calls for a repeat of the assessment. A repeat TB test will be performed one year after the date of the previous test (± 2 months). The repeat TB test can occur at any visit.

At every study visit, you will be asked about:

- any problems you are having,
- any side effects you are experiencing, which may or may not be related to the study,
- whether you have made any visits to other doctors or hospitals.

If you discontinue the study during the lead-in period, prior to randomization at Week 4, a short Early Termination visit is required for: returning study material and drug, assessing any safety/adverse events, collecting the reason for discontinuation. You will still have a 70-day follow-up call/visit; the remainder of study procedures can be completed per your physician's discretion.

After your final visit, you will have a follow-up phone call/visit approximately 70 days after the last administration of study drug to obtain information on any new or ongoing adverse events.

Optional Archived Samples

In this study, we also wish to collect additional blood samples to be used for future analysis of biomarkers. Biomarkers are substances sometimes found in an increased amount in the blood or other tissues and which can be measured and evaluated as indicators of disease activity and the likely course of rheumatoid arthritis, autoimmunity, and/or response to medications that treat your rheumatoid arthritis which may help researchers better understand the disease.

If you agree, an additional sample of 6 mL (approximately 1.2 teaspoons) of blood will be collected, frozen and stored in a centralized storage facility decided on by the sponsor (AbbVie) for up to 20 years. The samples will be used for testing RA related markers that can help to better understand and predict RA course and for future research related to your response to treatment. This will not involve insertion of an additional needle. None of these tests and markers are genetic. These tests will not help you directly, and the results will not be available to you or to your doctor or the study doctor. These tests may however, help patients in the future. These samples may be sent to AbbVie or companies AbbVie works with for testing, however, no one other than AbbVie, or people or companies that AbbVie works with, will test your samples. **You do not have to participate in the additional biomarker research for future analysis if you don't want to. You can still be in the study even if you don't want to be included in the**

additional biomarker research for future analysis. You may ask any questions before checking one of the boxes at the end of this form.

Your other blood and urine samples collected during the study will be destroyed as soon as testing is completed. You will not have to pay for any of the tests that are part of this biomarker research for future analysis. There will be no financial benefit to you in respect to any research results from the sample(s).

Optional Blood Sample for Pharmacogenetics Analysis

A separate consent form will explain this analysis and collection.

Subject Responsibilities

In order for this study to provide good information about how reduced dosing of adalimumab works in subjects with rheumatoid arthritis who are in clinical remission, you will be expected to do the following:

- Follow the instructions of your study doctor including requirements to use an appropriate birth control method.
- Come to all your scheduled study visits and procedures.
- You may be required to stop certain medications and supplements you are currently taking. Certain medications you are taking or have taken in the past may keep you from being in this study. Please review all of your medications with your study doctor.
- Some procedures/conditions you may have had in the past may keep you from being in this study.
- Take and store your study drug as instructed and return the unused study drug and/or empty containers to the study doctor's office at each visit. Your study doctor may withdraw you from the study if you do not take the study drug as instructed or if you provide false information about your study drug dosing.
- Do not share your study drug with anyone. You are the only person allowed to take the study drug.

- Keep the study drug and study supplies out of the reach of children and persons of limited ability to read or understand.
- Fill out your dosing sheet, questionnaires and/or diary completely and honestly and bring it to the study doctor's office at each visit.
- Do not change any of your rheumatoid arthritis medications or start any new rheumatoid arthritis medications without checking with your study doctor.
- Tell the study staff about any health problems you are having even if you don't think they are important.
- Contact the study staff anytime during this study if you think you have a flare.
- Tell the study staff if you wish to stop being in the study.
- Do not participate in any other research studies during your participation in this study.

You will receive a subject card stating that you are participating in the study. You must carry the 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.

In the event of an emergency, dial your local emergency phone number immediately.

If you require emergency care, be sure to tell the emergency care provider about your participation in this study. Contact the study doctor or study staff as soon as possible.

If you have questions about your participation in this study or if you think you have had a study-related injury or reaction to the study drug, or if you have any concerns or complaints about your participation in this study, contact the study doctor at the phone numbers listed on Page 1 of this Informed Consent Form. If an injection is missed, something occurs where the full dose cannot be injected or if you have any questions or concerns about the investigational product contact your study center immediately for further instructions.

If you have questions concerning your rights as a research subject, if you are not able to resolve your concerns with the study doctor or study staff, if you have a complaint, or if

you have general questions about what it means to be in a research study, you may contact:

[insert EC contact information]

Risks and Discomforts

Your study doctor will be monitoring you for side effects from adalimumab. It is important that you report any side effects you have had to your study doctor right away. Your study doctor may give you other drugs to help with side effects. If you or your study doctor thinks that you cannot tolerate the side effects, the study drug may be stopped altogether and you will be withdrawn from the study.

Ask the study doctor for the precautions and/or risks of Methotrexate.

Ask the study doctor if you have questions about the signs or symptoms of any side effects you read about in this consent form.

Please tell the study doctor or study staff right away if you have any side effects. Please tell them if you have any other problems with your health or the way you feel during the study, whether or not you think these are related to the study drug.

Adalimumab Risks

More than 29,000 subjects participating in rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, pediatric Enthesitis Related Arthritis, Crohn's disease, pediatric Crohn's disease, psoriasis, pediatric psoriasis, hidradenitis suppurativa, ankylosing spondylitis, non-radiographic axial spondyloarthritis, peripheral spondyloarthritis, psoriatic arthritis, intestinal Behçet's disease, uveitis and ulcerative colitis clinical studies have been treated with adalimumab. The majority of side effects experienced following administration of adalimumab were mild to moderate in severity.

Injection Site Reactions

The most common side effect of adalimumab injections was reaction at the injection site. Subjects had redness, itching, bruising, pain, and/or swelling at the injection site. Most injection site reactions were described as mild, transient, and the majority of these events resolved without stopping the drug.

Other Common Side Effects

Other frequently reported side effects of adalimumab in subjects participating in the clinical studies in order of decreasing frequency are: nasopharyngitis, upper respiratory tract infection, headache, nausea, diarrhea, bronchitis, cough, sinusitis, hypertension (increase in blood pressure), influenza (flu), urinary tract infection, back pain and rash.

Infection Risk

Infections were among the most common side effects seen with adalimumab in the clinical studies. The infections were primarily nasopharyngitis, upper respiratory tract infections (common colds), bronchitis, sinusitis, influenza (flu) and urinary tract infections.

Serious infections were also seen with adalimumab but were generally uncommon. These include: pneumonia, septic arthritis (infected joints), sepsis (infection within the bloodstream), post-surgical infections, cellulitis (skin infections), diverticulitis (infection of the colon), pyelonephritis (infection of the kidney), Legionellosis (a severe form of pneumonia), Listeriosis (infection usually caused by eating contaminated food) and opportunistic infections including invasive fungal (e.g., histoplasmosis) and parasitic infections. Other serious infections have also been reported. In adalimumab clinical studies there was higher number of serious infections seen in subjects over the age of 65. Serious infections may result in death.

Some subjects have developed active tuberculosis while taking adalimumab. This may indicate an activation of a previously inactive tuberculosis infection. Some subjects who have previously received treatment for latent or active tuberculosis have developed active

tuberculosis while being treated with adalimumab. If you have active tuberculosis, you should not enter the study.

Cases of relapse of Hepatitis B virus infection have occurred in patients taking TNF-blockers such as adalimumab.

You should not start adalimumab if you have any active infection. If you develop a new infection while on the study drug, your study physician will follow you closely. If the infection becomes serious, your study doctor may stop the study drug. If you have any symptoms of infection, whether you believe it is serious or not, please tell your study doctor.

You should not receive a vaccine that is described as "live" while taking adalimumab. There is no data available on the effects of live vaccines in patients receiving adalimumab. Prior to receiving any vaccination, check with your study doctor.

Cardiovascular Risk

There is a possibility that drugs that inhibit Tumor Necrosis Factor (TNF) may cause or increase the risk of congestive heart failure. If you have moderate to severe heart failure, you should not start adalimumab. Caution must be used in subjects with mild heart failure. If you have worsening of symptoms, shortness of breath or swelling of your ankles and feet, contact your study doctor immediately. At this time, the role of adalimumab in subjects with congestive heart failure is not known.

Cases of myocardial infarction (heart attack) and stroke (cerebrovascular [CV] accident) have been reported in subjects being treated with adalimumab.

Pulmonary Risk

Cases of interstitial lung disease (scarring and/or inflammation of the lungs), cases of pulmonary embolism (blood clots in the lung) and cases of pleural effusion (excess fluid in the space around the lungs) have been reported in patients taking adalimumab.

Neurologic Risk

There have been cases of nerve demyelination (breakdown of nerve cells) in subjects using adalimumab. An example of nerve demyelination is multiple sclerosis. Symptoms of demyelinating disease include numbness or tingling, problems with vision, weakness in legs and dizziness. It is not known if treatment with adalimumab has caused these side effects.

There have been cases of Guillain-Barré syndrome (a rare disorder in which the body's immune system attacks part of the peripheral nervous system) and optic neuritis (a disorder of breakdown of nerve cells in which loss of vision in one eye develops over the course of a few days) reported in patients taking adalimumab.

Cancer Risk

Adalimumab belongs to a class of drugs called TNF-blockers. In clinical studies of TNF-blocking agents, more cases of cancer including lymphoma and non-melanoma skin cancer have been observed among patients receiving TNF-blockers compared to patients who did not receive these drugs. There have also been cases of acute and chronic leukemia reported in association with the use of TNF-blockers including adalimumab. You should discuss these issues with your treating doctor.

Lymphoma is a type of blood cancer affecting the lymphatic system. Patients with rheumatoid arthritis, particularly those with highly active disease, may be at a high risk (many times higher than the normal rate in the general population) for the development of lymphoma. This high risk is inherent to RA. Very rare post-marketing cases of hepatosplenic T-cell lymphoma (HSTCL), another form of lymphoma, have been identified in patients treated with adalimumab. This rare type of T-cell lymphoma has a very aggressive disease course and has been fatal. The majority of the cases reported for adalimumab occurred in adolescent and young adult male patients with Crohn's disease or ulcerative colitis. Almost all the patients were taking or had taken other oral medications, e.g., azathioprine and 6-mercaptopurine, that can suppress the immune system at or prior

to diagnosis. It is uncertain whether the occurrence of HSTCL is related to the use of adalimumab or adalimumab in combination with these other drugs.

Non-melanoma skin cancers, which include basal cell carcinoma and squamous cell carcinoma of the skin, are usually non-life-threatening if caught early. Additionally, rare cases of Merkel cell carcinoma (a type of skin cancer) have been reported.

The more frequently observed cancers other than lymphoma and non-melanoma skin cancer observed during the use of adalimumab include breast, colon-rectum, uterine-cervical, prostate, lung, ovary, melanoma, thyroid, kidney, head/neck, stomach and other carcinomas. Some cancers may result in death.

Allergic Reaction Risk

Allergic reactions such as allergic rash and itching have been observed in approximately 2.9% of subjects taking adalimumab. In addition, there have been cases of erythema multiforme reported outside of the clinical trials. This is an allergic reaction caused by medication, illness or infection that presents as a red, splotchy rash on the body. Serious allergic reactions (e.g., Stevens-Johnson syndrome, anaphylaxis, angioedema) that can be life-threatening were observed rarely in people taking adalimumab. Before starting the study drug, you must tell your study doctor about any drug allergies. You should notify the study doctor right away if you have any allergy symptoms such as rash, hives, swelling, itching, shortness of breath, or trouble breathing.

The needle cover of the prefilled syringe contains dry rubber (latex). If you are sensitive to dry rubber (latex), please tell your study doctor before you start participating in this clinical study.

Hematological Risk

In adalimumab clinical trials anemia (low levels of red blood cells) has been observed commonly and leucopenia (low levels of white blood cells) uncommonly. Other blood disorders have been reported with adalimumab. These include thrombocytopenia (low

platelets) which is considered uncommon and pancytopenia (low counts of all blood cell types at the same time) which is considered rare. The relationship of these reports to the use of adalimumab is not known.

Other Adalimumab Risks

Formation of auto-antibodies, antibodies that develop against one's own cells or proteins, have been identified during adalimumab administration. In rare cases auto-antibody production, joint pain and rash can develop that appear similar to that seen in a disease called systemic lupus erythematosus (SLE) that is referred to as lupus-like syndrome. In most people these symptoms go away when adalimumab is stopped. SLE may affect internal organs. The role of treatment with adalimumab on the development of autoimmune diseases is unknown.

Cases of worsening or new onset of psoriasis (including palmoplantar pustular psoriasis) have been reported in subjects treated with adalimumab.

There have been cases of hair loss (alopecia) reported in both clinical trials as well as outside of clinical trials for adalimumab.

Other side effects that have been reported include fever, cutaneous vasculitis (inflammation of the blood vessels in the skin), sarcoidosis (an inflammatory disease of unknown cause that affects multiple organs in the body), and pancreatitis (an inflammation of the pancreas, a gland located behind the stomach that produces insulin).

The most common reasons that patients stop taking adalimumab are infections.

Abnormal laboratory test values seen in patients taking adalimumab include: high cholesterol, elevated fats (lipids) in the blood, blood in the urine, and increased liver enzymes. Liver problems like inflammation of the liver (hepatitis) may happen in people who use TNF-blocker medicine like adalimumab. These problems can lead to liver failure and death.

Deaths have occurred during treatment with adalimumab. The overall rate of death is not increased compared to normal death rates.

Certain medicines should not be used together because an interaction may occur. The use of adalimumab and other immune drugs such as anakinra (Kineret) or abatacept (Orencia) or other TNF-blockers is not recommended because patients taking the combination of adalimumab and either of these drugs may have an increased risk of infection and other potential interactions. Tell your health care professional if you are taking any other prescription or nonprescription (over-the-counter [OTC]) medicine.

Your study doctor will be monitoring you for side effects from adalimumab. It is important that you report any side effect experienced to your study doctor right away. Your study doctor may give you other drugs in order to keep side effects under control. If you or your study doctor feels that you cannot tolerate the side effects, the study drug may be stopped altogether and you will be withdrawn from the study.

Reproductive Risks

You may not take part in this study if you are breastfeeding, are pregnant, think that you may be pregnant, or are trying to get pregnant. If you are pregnant or breastfeeding, there may be risks to you and the baby that are not known at this time. Women who can get pregnant will be tested for pregnancy during the study. There is no information if adalimumab is safe for breastfeeding or unborn babies of mothers getting adalimumab.

You must avoid getting pregnant in order to take part in this research study. If you are sexually active you should use a method of birth control that is acceptable to you, the study doctor, and the sponsor. You must continue to avoid pregnancy for 150 days after your last dose of study drug.

If you are a man, there may be risks to an unborn baby you father during or after the study. Nobody knows what these risks are right now. Some drugs cause premature (early) birth or birth defects. The study doctor or study staff will talk to you about the

birth control options you and/or your partner must use during the study and for 150 days after you leave the study.

It is important for you to tell the study doctor at once if you or your partner get pregnant or think that you might be pregnant while you are in the research study. If you get pregnant, you will be asked to stop taking part in the study. If you or your partner becomes pregnant, the study doctor will discuss with you what you should do. It is recommended that women who have adalimumab treatment during pregnancy should not give their babies any live vaccines for at least 5 months after their last adalimumab injection during pregnancy. You may also be asked questions about your pregnancy and the baby even after the study is over.

[As applicable, per country requirements] Add privacy language for partner pregnancy data collected.

Unknown Risks

You might have side effects or discomforts that are not listed in this form. Some side effects may not be known yet. Tell the study doctor or study staff right away if you have any problems.

Risks Associated with Placebo

Some people in the study will get placebo instead of adalimumab. Receiving placebo is the same as not receiving anything for your rheumatoid arthritis. If you use placebo during the study, it is possible that your rheumatoid arthritis may get worse. Please ask the study doctor or study staff if you have any questions about placebo.

Risks Associated with Discontinuation

If you stop your regular medication to be in the study, your rheumatoid arthritis might come back or get worse. Please tell the study doctor or study staff right away if you have any problems or feel you are having a flare when you stop using your regular medication.

Other Risks Related to Study Procedures

Blood Draw Risks

You may have pain, bleeding or bruising at the site where the blood will be drawn. You may feel faint. An infection at the site where the blood was drawn is possible.

X-ray Risks

During x-rays you will be exposed to a small amount of radiation. The amount of radiation is not considered a significant risk.

MRI Risks

An MRI is a common medical imaging scan that uses magnetic forces to obtain detailed images of the body. MRI does not use radiation or x-rays. The presence of metal in your body may be a safety hazard or affect a portion of the MRI image. Be sure to mention to the technician if you have any of the following: metallic joint prostheses, artificial heart valves, an implantable heart defibrillator, a pacemaker, metal clips, cochlear implants, a bullet, shrapnel or any other type of metal fragments.

During an MRI, depending on the capabilities of the MRI scanner, you must lie motionless in the scanner, which is a confined space. This may occasionally produce anxiety or claustrophobia. The MRI scan will be performed on the hand and wrist most affected by rheumatoid arthritis (or on the dominant hand if both are equally affected). Gadolinium, a contrast agent will be injected into a vein from 10 and 30 seconds and most people will not notice anything. Rarely, people may have a cold feeling in the arm and mild nausea. Gadolinium contrast is generally safe and side effects or reactions are uncommon. The most common adverse reactions are brief headache, nausea (feeling sick) and dizziness for a brief time following the injection. Allergic (anaphylactic) reactions to gadolinium have occurred but are extremely rare. These severe reactions, which may involve difficulty breathing and swelling of the lips and mouth, occur in about 1 in every 10,000 people who have gadolinium. If you experience any of these reactions during or after the scan, please alert the MRI technician or staff immediately.

In subjects with normal kidney function most of the gadolinium contrast injected is almost entirely passed out in the urine within 24 hours.

Your study doctor will not recommend the contrast MRI if you have contra-indications such as severe renal insufficiency, severe hepatic insufficiency, and/or previous allergic reaction to gadolinium. Please inform your study doctor about these conditions.

Purified Protein Derivative (PPD) Skin Test Risks

A PPD skin test for tuberculosis (TB) involves the injection of a small amount of PPD fluid just under the skin in your forearm. You may have mild pain and/or a change in skin color from the needle stick. If you have a positive PPD skin test, you may experience pain, itching, redness, firmness, and swelling at the site of the skin test.

You will be asked to return to the study site within 48 – 72 hours after the test to have the test read. If the PPD skin test results are positive, you may be asked to have other tests performed (such as a chest x-ray).

A diagnosis of TB may be reportable to local health authorities according to local law.

Electrocardiogram (ECG) Risks

Skin irritation is rare but could occur during an ECG from the electrodes or gel that is used.

Ultrasound Risks

Ultrasound has no radiation so it does not have the same risks as an x-ray. There are no direct risks from an ultrasound exam. During the ultrasound exam a gel will be placed on the skin for ultrasound quality. It is possible to have skin irritation from the gel.

Questionnaires

Filling out the questionnaires could cause you to feel uncomfortable or upset. Please tell the study doctor or study staff if you feel uncomfortable or upset while filling out a questionnaire.

Costs

You will not be charged for the required study drug(s) (adalimumab, placebo) or procedures during the study. You are responsible for the cost of your regular medical care. Before you agree to be in this study, you should contact your healthcare payer/insurance company to see if your plan will cover the costs required as part of your participation. You can ask the study doctor or study staff to find out more about costs.

Subject Reimbursement of Travel Expenses

You will not be paid for your participation in this study. The **[insert proper EC term]** agreed that you may be reimbursed for travel expenses for study required visits. You will only be reimbursed for actual expenses incurred for each visit up to a maximum **[insert total dollar amount insert numeric number, local currency]**. If you do not complete the study, you will receive reimbursement only for the visits you have completed up to a maximum of **[insert dollar amount]** per visit. Reimbursement will be paid periodically. If you have any questions regarding your reimbursement for participation, please contact the study doctor at the telephone number listed on Page 1 of this consent document.

Benefits

The information that is obtained during this study may be useful scientifically and thus be helpful to others with the same condition in the future.

You may or may not receive any direct medical benefit from being in this study. Your condition may stay the same or it may get worse.

Alternatives to Participation

You do not have to participate in this study to receive and/or maintain treatment for your condition. You may maintain your current treatments since your RA is well controlled. If needed or recommended by your doctor, other alternatives to this study and further treatments for your rheumatoid arthritis may include other treatment strategies and/or other drugs already approved or are being used for the treatment of rheumatoid arthritis. Your study doctor can discuss the risks and advantages of these alternative treatment methods with you. In addition, you may discuss your options with your regular health care provider.

New Information

You or your legally authorized representative will be informed in writing in a timely manner and will be asked to sign a revised informed consent if new information that could affect your willingness to continue participation in this study becomes available.

In Case of Research Related Injuries

If, during your participation in this study, you are injured as a direct result of the study drug, AbbVie agrees to pay reasonable medical expenses necessary to treat the injury; provided you have followed the directions of the study doctor and to the extent you are not otherwise reimbursed by medical insurance. The study doctor and sponsor will determine whether any illness or injury is a direct result of the study drug or procedures performed for the purposes of the study. If you desire, you may arrange to have treatment performed by a licensed doctor selected by you, or, upon your request, AbbVie will arrange to have treatment provided by the study doctor or another licensed doctor. AbbVie makes no commitment to provide compensation except as described above. Be aware that your healthcare payer/insurer might not cover the costs of study-related injuries or illnesses. You will not lose any of your legal rights or release the Sponsor, the study doctor, the study staff, or study site from liability for mistakes or intentional misconduct by signing this consent document.

If you are injured during this study, your study doctor will discuss with you the available medical treatment options.

In the event of an emergency, seek immediate medical attention.

Confidentiality

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by US 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.

Data We Collect from You:

Your personal health information from your original medical records and all data resulting from your participation in this research will be collected during the course of this study. Your study doctor may ask you to sign a separate authorization to obtain some or all of your original medical records. Your personal health information could include physical examination details, as well as the results of any blood testing, x-rays, other medical procedures.

An electronic device will be used to collect your answers to questions regarding your health in your study doctor's office. If you experience a flare of your disease and enter into the open label rescue arm you will be given an electronic device to take home and answer questions about your health weekly. At the end of the study or if you withdraw from the study for any reason, you will be required to return the device to the site study staff. You may not use this device for any other reason than what is indicated in this document or allow others to use it.

How Your Data Will Appear:

Your identity and contact details will not be disclosed except as described in this form, unless required by law. Rather, your identity and contact details will be replaced by a code, such as a number.

Why We Collect this Data:

Your personal health information will be used for clinical research and may also be used for seeking approval from regulatory authorities to market the studied adalimumab. It may also be used in study reports or for scientific presentations, but in a way that will not identify you by name. Your personal health information will be kept confidential and, unless required by law, will not be made publicly available. After this study has been completed, it is possible that your coded health information will be used for future research.

Who Will See Your Data:

The only people with access to your personal health information in identifiable form will be the study doctor, personnel helping the study doctor conduct the study at the facility, sponsor, and its representatives who are checking that the study is conducted properly, ethics committee(s) and regulatory authorities where required by law.

You may not participate in this study unless you give your permission to use and disclose your personal health information. By signing this consent document you are allowing the study doctor and study personnel at the facility to permit AbbVie, its representatives, and others described in this form to have access to your personal health information for the purpose of collecting data, verifying the data is correct, and checking that the study is conducted properly.

In order to complete the research, AbbVie, its representatives, the study doctor and personnel at the facility, the **[insert proper EC term]** and local and foreign regulatory authorities responsible for overseeing research studies will have access to your coded health information.

Some of these organizations may be located outside of the country or region in which you live, including in countries where data protection requirements may be different or less restrictive than in your home country or region. However, AbbVie will take reasonable measures to keep your personal health information confidential. However, absolute

confidentiality cannot be guaranteed. By signing this document, you agree to the transfer of your personal health information to such countries, including the United States. If the results of the study are published your identity will remain confidential.

Taking Back Your Permission to Use or Disclose Your Personal Health Information:

To take back your permission to use or disclose your personal health information you must write to your study investigator at the address listed on Page 1 of this consent form. If you do this, you will no longer be allowed to be in this study. Any information that has already been collected at the time you take back your permission will be kept and, where the law allows, your personal health information, will continue to be used by the study doctor or AbbVie or other parties involved with the study.

No new data will be collected about you after you withdraw from the study.

Rights to Your Data:

You may have the right to access, correct and make a copy of your medical and/or clinical study records as allowed by applicable privacy laws. You may ask to see your records by requesting such records from the study doctor or the facility(ies) where the study is being conducted. However, to ensure the valid results of the study, you agree that you may not be able to review or make a copy of some of your records related to the study until after the study has been completed.

When you, or your legal representative, sign this document, you agree to the access, collection, processing and transfer of your personal health information as described in this informed consent document. If you do not sign this form, you cannot be in the study.

Withdrawal/Voluntary Participation

Participation in this study is voluntary. You can stop participating in the study at any time. If you decide not to participate in the study or to withdraw from the study, the quality of your medical care or any benefits to which you are otherwise entitled will not be affected and there will be no penalty to you. Your study doctor may also end your

participation in the study if he/she believes that it is in your best interest or if you are unable to follow the requirements of the study. In addition, AbbVie may end your participation in the study at any time without your consent.

When you withdraw from the study for any reason, all pre-filled syringes and pre-filled syringe boxes, including those unused and empty or used pre-filled syringe sharps containers (unless prohibited by law) as well as an electronic device (if you received it) must be returned to the study site. You will also be asked to return to the study site so that the study doctor may perform a final evaluation, which may include a physical examination and/or laboratory tests.

[For EU sites] Please insert a description of the arrangement for care of the subjects after their participation in the study has ended.

[As applicable, per country requirements] Please insert requirements regarding collection, shipping and storage of samples.

Consent

I have read and understand this consent form and its contents were explained. My questions have been answered to my satisfaction. I consent voluntarily to participate in this research study and I or my legally authorized representative will receive a signed and dated copy of this consent form for my records.

Please check one box for the Optional Biomarker Research for Future Analysis:

☐ Yes, I would like to participate in the optional additional biomarker research for future analysis

☐ No, I would not like to participate in the optional additional biomarker research for future analysis

By signing this consent form, I am not giving up any of my legal rights.

By signing this informed consent form, I am authorizing access, use and transfer of my personal data as described in this informed consent.

Name of Subject (Printed)

Signature of Subject Date

I attest that the subject named above (and/or legally authorized representative named below) had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to be in this study.

Name of Person Conducting Informed Consent Discussion (Printed)

Signature of Person Conducting Informed Consent Discussion | Date

I certify that under applicable law I am the legally authorized representative of the subject named above and that I am authorized to sign this consent to his/her participation in the research study described above. I am also authorizing the access, use and transfer of the subject's study-related records as described above.

Name of Legally Authorized Representative (Printed)

Signature of Legally Authorized Representative | Date

The study subject has indicated that he/she is unable to read. The consent document has been read to the subject by a member of the study staff, discussed with the subject by a member of the study staff, and the subject has been given an opportunity to ask questions of the study staff.

Name of Impartial Witness (Printed)

Signature of Impartial Witness* Date

* Impartial Witness: A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject's legally authorized representative cannot read, and who reads the informed consent and any other written information supplied to the subject.