Title: Anakinra for the Treatment of Chronically Inflamed White Matter Lesions in Multiple Sclerosis

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PRINCIPAL INVESTIGATOR: Daniel Reich, MD, PhD

STUDY TITLE: Anakinra for the Treatment of Chronically Inflamed White Matter Lesions in Multiple Sclerosis (ATaC-MS)

STUDY SITE: National Institutes of Health

Cohort: Standard

Consent Version: 10/19/2022

WHO DO YOU CONTACT ABOUT THIS STUDY?

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KEY INFORMATION ABOUT THIS RESEARCH

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). This section provides the information we believe is most helpful and important to you in making your decision about participating in this study. Additional information that may help you decide can be found in other sections of the document. Taking part in research at the NIH is your choice.

- Participation in this research study is voluntary.
- In this study, we will test whether a drug called anakinra can reduce inflammation in multiple sclerosis (MS) brain lesions. This type of inflammation is not treated by available medications for treatment of multiple sclerosis.
- Anakinra is an FDA approved drug, used for the treatment of some immune system mediated diseases, such as rheumatoid arthritis. This medication reduces the function of a certain type of immune cell that contributes to brain inflammation. We will use this medication in the doses that have been approved for the other indications.
- This study will take approximately 24 weeks from the time you enroll. You will not be able to participate in any other treatment research studies during this time.
- If you qualify for the study and decide to participate, you will undergo scheduled visits at NIH.
- You will not be able to participate in this study if you have metal in your body or if you are pregnant. Other exclusions apply and will be discussed with you during your baseline visit.
- There will be 4 study visits while you are taking anakinra and then 2 follow-up visits after you stop taking anakinra. At each study visit, you will have a clinic exam, bloodwork, and brain MRI.

- Brain MRIs are being performed for safety and a gadolinium guide will be provided to you.
- A lumbar puncture will be performed 3 times during this study at the Baseline, Week 12, and Week 24 study visit.
- Anakinra is given as a daily subcutaneous (under the skin) injection. You will be taught how to give yourself these injections.
- Your starting dose of anakinra will be 100 mg daily. As long as you tolerate the injections, every 4 weeks the dose of the injections will be increased up to the maximum dose of 300 mg daily.
- If treatment is stopped early for whatever reason, you will still have 2 post-treatment follow-up visits at week 4 and 12 after stopping the drug.
- All of the information collected during this study will be stored for future analysis. This includes clinical information, MRIs, blood and cerebrospinal fluid samples.
- All study-related visits will take place in the outpatient clinic of the NIH Clinical Center and may last up to one full day. For convenience, you and the study team may choose to split your visits over several days or to have a study visit as inpatient in the NIH Clinical Center.
- After you complete study participation, continued medical care will not be offered at NIH and you will return to the care of your primary outside provider. If you are eligible, you may choose to participate in other Neuroimmunology Studies at NIH.
- The risks or discomforts of being in study are explained in detail in this consent form.
- The common side-effects of anakinra are:
    - Skin reaction at the site of injection
    - Upper respiratory tract infection
    - Headache
    - Nausea
    - Diarrhea
    - Sinusitis
    - Joint aches
    - Flu-like symptoms
    - Abdominal pain
    - Allergic reaction
- On rare occasions, anakinra may cause liver toxicity. This is reversible. Anakinra may also increase your risk of infections.
- You may or may not receive direct benefit from participating in this research study. From your participation in this study, we also hope to learn more about multiple sclerosis and whether or not we can treat chronic inflammation in multiple sclerosis with anakinra.
- You may choose not to take part, or you may leave the study at any time, for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation. Additionally, if you choose to leave the study, please inform your study team.
- We will not compensate you for time and research-related inconveniences.

- We may provide travel and/or lodging compensation if you will be coming from out-of-town or if traveling to NIH for you is a hardship. In such cases, an escort fee may be provided.

The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time you need to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

This is a research study. The purpose of this study is to see if a drug called anakinra can help clear inflammation in multiple sclerosis lesions.

This drug is approved for use in rheumatoid arthritis; however, it is not approved by the FDA for the treatment of multiple sclerosis and therefore is considered investigational for this research.

Some multiple sclerosis lesions remain inflamed for very long periods of time (sometimes years). This type of inflammation is not affected by any of the available multiple sclerosis medications. We can see these lesions using advanced MRI scans. Research has shown that these lesions can lead to slow clinical worsening of symptoms in multiple sclerosis (often called “progressive MS”). In this research study, we will test whether anakinra can help clear the inflammation in these lesions by seeing if anakinra can change how the plaques appear on MRI.

We are asking you to join this research study because we think you may be a good candidate for this trial.

WHAT WILL HAPPEN DURING THE STUDY?

If we think you can be included in this study and you are willing and able to take part, you will be asked to come to the NIH for a baseline visit. The baseline visit may take place over a few days.

During the baseline visit, we will do the following research procedures:

1) Clinical evaluation
2) Blood and possibly urine testing
3) MRI of the brain

4) Lumbar puncture

Once all baseline procedures are completed, and it is confirmed you are eligible to participate in this study, you will begin treatment with the study drug (anakinra). You will receive your first dose of anakinra in the clinic. We will teach you (and your caregiver) how to administer a subcutaneous injection. We will give you your first 4-week supply of anakinra at the starting dose of 100 mg to take at home. You will be given a sharps box to dispose of your used syringes. We will ask you to save all your empty drug vials to be returned to us at your next visit. We will provide you with a drug diary, that you can choose to use to log daily drug administration and any notes on side effects. We will contact you 1 to 2 days after your first dose of anakinra to ask about any side effects.

You will return for your next study visit at week 4. At that time, we will collect your sharps box and empty drug vials. If you are doing well with anakinra injections, we will give you your second 4-week supply and a new sharps box. Your second supply will be at the next dose of 200 mg. You will administer anakinra 200 mg daily at home for 4 weeks. You will then return for your week 8 visit. At that time, we will collect your sharps box and empty drug vials. If you continue to do well, at your week 8 visit, you will receive your next 4-week supply of anakinra and a new sharps box. This supply will be 300 mg per day. You will administer anakinra 300 mg daily at home. You will then return for your week 12 visit. At that time, we will collect your sharps box and empty drug vials. After this visit, you will stop treatment with anakinra. After you stop treatment, you will have 2 more follow-up visits at week 16 and week 24. Details of what will happen at each study visit are in the table below.

Procedure	Study visit	Baseline (within 14d)	1–2d after baseline	Week 4 (±7d)	Week 8 (±7d)	Week 12 (±7d)	Week 16 (±7d)	Week 24 (±7d)
Clinic visit with physical exam		X		X	X	X	X	X
Laboratory testing		X		X	X	X	X	X
Clinical scales		X				X		X
Phone call			X					
MRI		X		X	X	X	X	X*
Lumbar puncture		X				X		X
Anakinra supply		X		X	X			

*Week 24 MRI will be performed without gadolinium (unless needed for clinical reasons)

If you miss a dose of anakinra, you must inform the study team. You will restart the next day with the same dose. You should never inject a higher dose or more than one dose per day.

If you request, you may be contacted via email to schedule appointments.

We may access data in your medical record that was collected under other protocols and use it for research in this study, so you do not have to repeat procedures/tests. If you are co-enrolled in another NIH protocol, then research data and/or specimens, collected in either study, may be shared with and used for research in either study, with IRB approval

History and examination, including clinical scales

We will ask you about your medical history and do a physical examination. This physical examination is for research purposes only and does not replace any examination you may receive from you own physicians.

Blood work

You will have blood drawn from a vein. This may require a needle stick in your arm or hand, or if you already have an IV catheter in place, we may be able to draw through that. Blood will be collected both for clinical monitoring and for research purposes. Details of the blood draw are in the table below.

Visit	Blood volume (teaspoons)
Baseline, Week 12, Week 24	12
Week 4, Week 8, Week 16	10

The amount of blood drawn cannot exceed 37 tablespoons over an 8-week period for research. Please tell the study staff if you are participating in other studies that have blood draws.

Urine testing

We will collect less than 1 cup of urine to test for possible pregnancy in women of childbearing potential. Urine pregnancy test will be done before every MRI and before getting your first dose of anakinra.

MRI

Magnetic resonance imaging (MRI) uses a strong magnetic field and radio waves to take pictures of the body. We will obtain pictures of your brain, spinal cord or optic nerves for this study. The MRI scanner is a metal cylinder surrounded by a strong magnetic field. The MRI scanner is a metal cylinder surrounded by a strong magnetic field. During the MRI, you will lie on a table that can slide in and out of the cylinder. You will be in the scanner for about 120 minutes. While in the scanner you will hear loud knocking noises, and you will be fitted with earplugs or earmuffs to muffle the sound. You will be able to communicate with the MRI staff at all times during your scan, and you may ask to be moved out of the machine at any time.

We will be using the MRI for investigational research. This means that the way the MRI is generating the images may be different than what is normally done in a routine clinical scan. However, all studies done under this protocol will be performed within FDA safety guidelines. Some of the MR machines that we use are considered investigational (not yet approved by the FDA for this use) but are used within the FDA safety guidelines.

During part of the MRI you will receive gadolinium, a contrast agent, through an intravenous (iv) catheter (small tube). It will be done for research purposes.

It is not known if MRI with contrast is completely safe for a developing fetus. Therefore, all women of childbearing potential will have a pregnancy test performed no more than 24 hours before each MRI scan with contrast. The scan will not be done if the pregnancy test is positive.

Lumbar puncture

You will undergo a lumbar puncture (sometimes called a "spinal tap") to obtain cerebral spinal fluid (CSF) samples at the baseline and week 28 visits. This procedure involves inserting a small needle into your lower back. The study staff will help position you either on your side or sitting up. The lower part of your back will first be cleaned with antiseptic, and then the study doctor will inject a small amount of local anesthetic to numb the area. Once numb, a very thin needle will be inserted into the spinal canal in your lower back [well below where the spinal cord ends]. About 1 ½ teaspoons of spinal fluid will be removed for analysis and storage. Your body usually replaces this fluid within 1-2 hours.

After the lumbar puncture is complete, you will be monitored for about 30 minutes. To prevent side effects, it is important that you not do any strenuous physical activity for 24 hours following the procedure. This includes lifting, bending, doing housework and gardening, or exercising.

Study Drug: Anakinra

We will give you a 4-week supply of anakinra at your baseline visit, week 4, and week 8 visits. The starting dose will be 100 mg every day for the first 4 weeks. Every 4 weeks we will increase the dose by 100 mg. We will not increase the dose if you experience side effects of the medication or if the lesions on your MRI already appear improved at the lower dose. You will take anakinra by injecting it under your skin. We will give you instructions on how to inject this medication before the first dose.

HOW LONG WILL THE STUDY TAKE?

The study lasts about 24 weeks from the time you enroll. You will have a baseline visit; three visits while taking anakinra and then two follow up visits after you have stopped taking anakinra. Visits will last 4-6 hours.

If you are interested and eligible, you may be followed under another Neuroimmunology Clinic protocol.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have 10 people participate in this study at the NIH.

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?

History and examination, including clinical scales

There is minimal medical risk or discomfort from the physical exam

Blood work

Blood draws may cause pain, redness, bruising or infection at the site of the needle stick. Rarely some people faint. The study team member may apply numbing cream to the area so that the needle stick won't hurt as much.

Urine collection

There is minimal medical risk or discomfort from giving a urine sample.

MRI

People are at risk for injury from the MRI magnet if they have some kinds of metal in their body. It may be unsafe for you to have an MRI scan if you have pacemakers or other implanted electrical devices, brain stimulators, some types of dental implants, aneurysm clips (metal clips on the wall of a large artery), metal prostheses (including metal pins and rods, heart valves, and cochlear implants), permanent eyeliner, tattoos, an implanted delivery pump, or shrapnel fragments. Welders and metal workers may have small metal fragments in the eye. You will be screened for these conditions before having any MRI scan. If you have a question about metal in your body, you should inform the staff. You will be asked to complete an MRI screening form before each MRI scan you have.

In addition, all magnetic objects (like watches, coins, jewelry, and credit cards) must be removed before entering the MRI scan room.

People with fear of confined spaces may become anxious during an MRI. Those with back problems may have back pain or discomfort from lying in the scanner. The noise from the scanner is loud enough to damage hearing, especially in people who already have hearing loss. Everyone having a research MRI scan will be fitted with hearing protection. If the hearing protection comes loose during the scan, you should let us know right away.

In this study, we are using an MRI scanner that has a strong 7 tesla magnet. Because of the strong magnetic field, some people have brief periods of muscle twitching, eye discomfort, dizziness, mild nausea, headache, a metallic taste in their mouth or a sensation of flashing lights. Many of these effects are from moving too quickly in the magnetic field, so you will be asked to walk slowly to the MRI table. Once you lie down, we will move the table slowly into the scanner. You can ask us to stop the scan at any time if you feel too uncomfortable. There is no evidence that scanning at high magnetic field strengths is dangerous, but we do not know if there are any long-term effects.

There are no known long-term risks of MRI scans.

The risks of an IV catheter include bleeding, infection, or inflammation of the skin and vein with pain and swelling.

Mild symptoms from gadolinium infusion occur in fewer than 1% of those who receive it and usually go away quickly. Mild symptoms may include coldness in the arm during the injection, a metallic taste, headache, and nausea. In an extremely small number, fewer than one in 300,000 people, more severe symptoms have been reported including shortness of breath, wheezing, hives, and lowering of blood pressure. You should not receive gadolinium if you previously had an allergic reaction to it. You will be asked about such allergic reactions before gadolinium is given.

People with kidney disease are at risk for a serious reaction to gadolinium contrast called "nephrogenic systemic fibrosis (NSF)". This condition always involves the skin and can also involve the muscles, joints and internal organs. NSF has resulted in a very small number of deaths.

A blood test of your kidney function may be done within the month before an MRI scan with gadolinium contrast. You will not receive gadolinium for a research MRI scan if your kidney function is below the safe level.

Most of the gadolinium contrast leaves the body in the urine. However, the FDA has issued a safety alert that indicates small amounts of gadolinium may remain in the body for months to years. The effects of the retained gadolinium are not clear. At this time, retained gadolinium has not been linked to health risks in people whose kidneys work well. Some types of gadolinium contrast drugs are less likely to remain in the body than others. In this study, we will use the gadolinium contrast drugs that are less likely to remain in the body, whenever possible. We will also give you additional information called a "Medication Guide." Upon request, we will give you individual information about retained gadolinium we see on your studies.

Lumbar puncture (spinal tap)

The lumbar puncture may cause pain at the site where the needle goes in and the spinal fluid is taken. There is a small risk of infection or bleeding. After the lumbar puncture you may get a headache. About a third of adults report a headache after an LP. To minimize the risk of a headache, the doctor will use a small needle and may prescribe bed rest for one or more hours after the procedure. If a headache occurs, it is usually mild and can be controlled by bed rest, drinking lots of fluids and a pain pill, such as acetaminophen. Rarely, the headache is severe and may require additional treatment with a "blood patch". In this procedure, a small amount of your own blood is injected into the lumbar puncture site. This procedure is generally effective in stopping the headache. A rare but serious complication of a LP, if it is done when the pressure inside the head is higher than normal (such as when a brain tumor is present), is known as medullary herniation which can result in death. Increased intracranial pressure is very unlikely to be present. The LP will not be done if there are any clinical indications that you have increased intracranial pressure, a skin infection in the lower back area, or bone malformation of the lower back (including severe scoliosis) which would make a LP difficult.

To minimize these risks, the lumbar puncture procedure will be performed by a medical professional specifically trained to do this procedure.

Contraception

The risks of anakinra administration on your ability to become pregnant and on a fetus is not known. Therefore, people who are planning to become pregnant should not enter this study, and participants who are physically able to get pregnant must use effective contraception (birth control) or remain completely abstinent from sexual intercourse from the time you enroll in the study until 12 weeks after your last dose of anakinra (Week 24 of the study).

Effective methods of birth control for this study include:

1) Hormonal contraception (birth control pills, injected hormones or vaginal ring)

2) Intrauterine device

3) Barrier methods (condom or diaphragm) used with spermicide

4) Surgical sterilization (hysterectomy, tubal ligation, or vasectomy of a partner)

It is important for you to know that no method of birth control is totally effective in preventing pregnancy except for surgical sterilization (hysterectomy, tubal ligation or partner's vasectomy) or total abstinence from sexual intercourse.

Study Drug: Anakinra

Anakinra is given by a shot under the skin. Most people take anakinra without any problems. The common side-effects of anakinra are listed below. If you have any of these, you should tell our study team right away:

- Skin reaction at the site of injection
- Upper respiratory tract infection
- Headache
- Nausea
- Diarrhea
- Sinusitis
- Joint aches
- Flu-like symptoms
- Abdominal pain
- Allergic reaction, rarely severe

On rare occasions, anakinra may cause liver toxicity. This is reversible. While you are in this study, we will monitor your liver function tests. Anakinra may also increase your risk of infections. For this reason, we will monitor your white blood cell counts. Before starting a new medication during this study, you must notify the research team to make sure it is safe with anakinra.

What are the risks related to pregnancy?

Anakinra has not been studied in pregnant women. The risks to pregnant women and unborn children are not known. For this reason, you may not participate in this study if you are pregnant.

If you are able to become pregnant, we will ask you to have a pregnancy test before starting this study and before any brain MRI or exposure to radiation (for example, if your lumbar puncture is done with x-ray guidance. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time. You must use effective birth control methods and try not to become pregnant while participating in this study. If you become pregnant, there may be unknown risks to the fetus or unborn child, or risks that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to a fetus. You must tell the study doctor if your birth control method fails while you are in the study. If you think or know you have become pregnant while participating in this research study, please contact the study team as soon as possible. If you plan to become pregnant in the future, please discuss with the study team how long you need to wait before becoming pregnant after completing the course of this study drug or procedures on this study.

If you are a sexually active person with a partner able to become pregnant, it is important that your partner not become pregnant during your participation in this study. There may be unknown risks to a fetus or risks we did not anticipate. You and your partner must agree to use birth control if you want to take part in this study. If you think your partner has become pregnant during your participation in this study, please contact the study team as soon as possible. If you and your partner plan for your partner to become pregnant after your participation in this study, please discuss this with the study team.

What are the risks of radiation from being in the study?

What if you are pregnant? If you are pregnant or nursing, you cannot be in this research study because the radiation may harm your baby. If you are nursing a baby, please tell your doctor. If you are able to have a baby and are not pregnant now, and you want to be in this study, we will give you a pregnancy test. If you join in this study, you should use contraception to keep from getting pregnant while you are in the study. If you get pregnant while you are in this study, or if you think you are pregnant, please tell the study doctor right away.

During your participation in this research study, you may be exposed to radiation from a lumbar puncture performed under x-ray guidance. This is considered a low exposure. The risk of this exposure is too low to be reliably measured.

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. This type of radiation is called "background radiation". No one knows for sure whether exposure to these low amounts of radiation is harmful to your body. The radiation you will get by participating in this study is less than the average yearly background radiation in the United States.

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You might not benefit from being in this study.

However, the potential benefit to you might be if anakinra helps clear inflammation in multiple sclerosis lesions. If anakinra has no effect on multiple sclerosis inflammation in the brain, you may not benefit. Even if anakinra reduces brain inflammation, this may not improve your symptoms.

Are there any potential benefits to others that might result from the study?

In the future, other people might benefit from this study because we may be able to learn more about multiple sclerosis, how we can best study inflammation in multiple sclerosis, and whether or not we can treat inflammation in multiple sclerosis with anakinra..

WHAT OTHER OPTIONS ARE THERE FOR YOU?

Before you decide whether or not to be in this study, we will discuss other options that are available to you. Instead of being in this study, you could choose to continue treating your multiple sclerosis as you are now. Because anakinra is FDA approved for the treatment of other conditions, you could receive it without taking part in this research study.

DISCUSSION OF FINDINGS

New information about the study

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

Return of research results

We may discuss the results of the research tests with you. If we learn information during this study that may be important for your health, we will share that information with you.

EARLY WITHDRAWAL FROM THE STUDY

We may stop your participation in the study if:

- You are unable to come to the study visits
- You are unable to tolerate the medication due to significant side effects
- You develop a clinical relapse
- You develop new or gadolinium-enhancing lesions on MRI
- You become pregnant
- Your MRI shows that your chronically inflamed multiple sclerosis plaques have resolved

If you take anakinra for any length of time during the course of this study, even if you do not finish the full 12 weeks of treatment, we will ask that you come back for 2 follow-up visits after the last dose.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

Will your specimens or data be saved for use in other research studies?

As part of this study, we are obtaining blood, specimens and data from you. We will remove all the identifiers, such as your name, date of birth, address, or medical record number and label your specimens and data with a code so that you cannot easily be identified. However, the code will be linked through a key to information that can identify you. We plan to store and use these specimens and data for studies other than the ones described in this consent form that are going on right now, as well as studies that may be conducted in the future. These studies may provide additional information that will be helpful in understanding multiple sclerosis, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to the development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you.

I give permission for my coded specimens and data to be stored and used for future research as described above.

_____Yes _____No

Initials Initials

Will your specimens or data be shared for use in other research studies?

We may share your coded specimens and data with other researchers. If we do, while we will maintain the code key, we will not share it, so the other researchers will not be able to identify you. They may be doing research in areas that are similar to this study or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or commercial entities.

I give permission for my coded specimens and data to be shared with other researchers and used by these researchers for future research as described above.

_____Yes _____No

Initials Initials

If you change your mind and do not want us to store and use your specimens and data for future research, you should contact the research team member identified at the top of this document. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your specimens and data. For example, if some research with your specimens and data has already been completed, the information from that research may still be used. Also, for example, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw them.

In addition to the planned use and sharing described above, we might remove all identifiers and codes from your specimens and data and use or share them with other researchers for future research at the NIH or other places. When we or the other researchers access your anonymized data, there will be no way to link the specimens or data back to you. We will not contact you to ask your permission or otherwise inform you before we do this. We might do this even if you answered "no" to the above questions. If we do this, we would not be able to remove your specimens or data to prevent their use in future research studies, even if you asked, because we will not be able to tell which are your specimens or data.

NIH policies require that your clinical and other study data be placed in an internal NIH database that is accessible to other NIH researchers for future research. Usually, these researchers will not have access to any of your identifiers, such as your name, date of birth, address, or medical record number; and your data will be labeled with only a code. We cannot offer you a choice of whether your data to be placed in this database or not. If you do not wish to have your data placed in this database, you should not enroll in this study.

How long will your specimens and data be stored by the NIH?

Your specimens and data may be stored by the NIH possibly indefinitely.

Risks of storage and sharing of specimens and data

When we store your specimens and data, we take precautions to protect your information from others that should not have access to it. When we share your specimens and data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your specimens and data.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

This study will offer reimbursement for, or payment of, travel or lodging if you will be coming from out-of-town or if traveling to NIH for you is a hardship. In such cases, an escort fee may be provided.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- You will receive study treatment at no charge to you. This may include medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH)
- Medicines that are not part of the study treatment will not be provided or paid for by the Clinical Center, NIH.
- Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

CONFLICT OF INTEREST (COI)

The NIH reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a COI Guide. You may ask your research team for a copy of the COI Guide or for more information. Members of the research team who do not work for NIH are expected to follow these

guidelines or the guidelines of their home institution, but they do not need to report their personal finances to the NIH.

The National Institutes of Health and the research team for this study have developed imaging techniques being used in this study. This means it is possible that the results of this study could lead to payments to NIH. By law, the government is required to share such payments with the employee inventors. You will not receive any money from the development of imaging techniques.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Data will be stored using codes that we assign and will be kept in password-protected computers.

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The study Sponsor National Institute of Neurological Disorders and Stroke
- Qualified representatives from Swedish Orphan Biovitrum, the pharmaceutical company who produces anakinra.

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical information that we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Daniel Reich, MD, (301) 496-3825, daniel.reich@nih.gov. Other researchers you may call are: Shari Sawney, MS at (301) 496-3825. You may also call the NIH Clinical Center Patient Representative at 301-

496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness should sign below if either:

1. **A short form consent process has been used to enroll a non-English speaking subject or**
2. **An oral presentation of the full consent has been used to enroll a blind or illiterate subject**

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

_____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.