Informed Consent Cover Page for FDAAA consent posting:

Official Title:	Single Patient Study of JAK/STAT Inhibition in CNS Kohlmeier-Degos Disease
NCT number:	NCT05998395
Document Type:	Informed Consent Form (Standard)
Document Date:	8/20/2024

PRINCIPAL INVESTIGATOR: Cornelia Cudrici, M.D.

STUDY TITLE: Single Patient Study of JAK/STAT Inhibition in CNS Kohlmeier-Degos Disease

STUDY SITE: NIH CC

Cohort: Standard

Consent Version: 08/20/2024

WHO DO YOU CONTACT ABOUT THIS STUDY?

PI: Cornelia Cudrici, M.D., cudricicd@mail.nih.gov, 240-515-5540

Study Coordinator: Jayson Grey, RN, jayson.grey@nih.gov, 301-402-9841

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.

The purpose of this research study is to find out if a drug called ruxolitinib (study drug) is safe and if it will control your brain and spine lesions due to Kohlmeier-Degos (KD) disease. Ruxolitinib is a drug that is FDA approved to treat several diseases including myelofibrosis and graft-versus-host disease. Ruxolitinib is not approved by the FDA to treat KD disease so this is an investigational study. We plan to add ruxolitinib to your current treatment plan, so you should continue to take your normal medications while taking ruxolitinib.

We will give you the same dose of this medication that has been approved and shown to be safe for other diseases.

During this study you may have up to 7-8 visits which may include:

Medical History and Physical exam
Review of Medications you take
Taking your vital signs
Blood draw
Brain and Spine MRI with contrast
Neurological Consult
Lumbar puncture (spinal tap)
Skin biopsies
Pill counts
Review of adverse events (AE)
Determining whether to continue the study drug or change your dose

Potential known risks related to this research study include:

Risks of study procedures: pain, discomfort, and bruising are the most frequent complaints at the site of the lumbar puncture, skin biopsy or blood draw, with some people experiencing bleeding or rare infections. You could have a spinal headache after the lumbar puncture.

Risks and common side effects from taking ruxolitinib may be low blood counts, including low platelets, red blood cells, neutrophils, infections, and lipid elevations (such as cholesterol).

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:

- Continue your current medication and treatment or;
- You may choose to take part in a different study here or somewhere else if there is one available.

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 interventions in which they would want to participate. 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.

If the individual being asked to participate in this research study is not able to give consent for themselves, you, as the Legally Authorized Representative, will be their decision-maker and you are being asked to give permission for this person to be in this study. For the remainder of this document, the term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research.

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?

We are asking you to join this research study because you have Kohlmeier-Degos disease with abnormalities on your brain and spine. There is no proven effective treatment. Based on tests that we did in the lab, we believe ruxolitinib may help decrease the inflammation in your body, particularly in the brain and spinal cord.

WHAT WILL HAPPEN DURING THE STUDY?

If you agree to participate in the study your participation will last up to 77 weeks.

During the initial visit, which we will call Visit 1, you will talk with us about the nature of this study and confirm your eligibility and sign this consent. After you have signed the consent but before you start the study drug, we will run tests that may involve the following:

- review of medical history
- physical examination with vital signs
- brain and spine MRI
- lumbar puncture to collect cerebral spinal fluid (CSF)
- skin biopsies
- blood draws
- visit with a neurologist

After we have done these evaluations, you will begin taking ruxolitinib. We will give you instructions on how to take the medication and what to do if you missed a dose.

It is important that you tell us of any side effects, symptoms or illness you have while taking the medication, especially any signs or symptoms of infection such as fever, chills, nausea, fatigue or urinary symptoms.

We may call you on the phone in between your visits to make sure you are taking the medication correctly, doing well and if you are having any side effects. We ask that you tell us if you develop any symptoms or illnesses while in the study. We may ask you to come in for an additional, unscheduled study visit in this situation to evaluate your symptoms if we feel this is necessary.

You will be asked to come to the NIH Clinical Center for planned visits which are described in the table below. These visits may be inpatient or outpatient visits and may take place over several days.

Once you have completed the baseline testing, you will start taking the drug as follows:

- 5 mg (one 5 mg tablet, tablet has “5” on it) twice a day for 1 week (7 days)
- 10 mg (one 10 mg tablet, tablet has “10” on it) twice a day, starting after Visit 2, for 13-73 weeks (91- 511 days)
- 5 mg (one 5 mg tablet, tablet has “5” on it) twice a day for 1 week (7 days)

If by any chance you do not tolerate the highest dose, we will adjust your dose so that you can continue to take the study drug at the dose that gives you the least side effects.

If you have to temporarily stop the drug for any reason and the team believes you can restart the drug safely, you may be on study a little longer to make up for the dates you did not take the study drug.

Please see Schedule of Activities below or on following page.

Schedule of Activities:

Visits may occur either in person in NIH or via Telehealth platform. For Telehealth visits you don’t have to travel to NIH. Visits that include MRI, Lumbar puncture and Skin biopsy should be performed in NIH; for these procedures we need to see you in NIH.

	Visit 1: Baseline (Week 0)	**Visit 2: (Week 1) Telehealth Visit**	**Visit 3: (Week 4) Telehealth or in person**	**Visit 4*: (Week 13)**	**Visit 5: (Week 14) Telehealth Visit or in person**	**Visit 6: (Week 25)**	**Visit 7**: End of Week 49**	Visit 8**: End of week 61 (+/- 7 days) Telehealth visit	Continuation Visit 9**: Up to the end of week 73 or End of Treatment	**Safety Visit*** 4 weeks after last dose of study drug. Telehealth Visit or in person**
Informed consent	X	-	-	-	-	-	-	-	-	-
History/Physical	X	-	X	X	-	X	X		X	X
Review of Medications	X	-	X	X	-	X	X		X	-
Vital signs	X	-	X	X	-	X	X		X	X
Blood draw	X	X	X	X	-	X	X	X	X	X
Brain /Spine MRI with contrast	X	-	-	X	-	X	X	-	X optional	-
Neurological Consult	X	-	X	X	-	X	X	-	X	-
Lumbar puncture	X	-	-	X	-	X	X	-	X optional	-
Skin biopsies	X	-	-	X	-	X	X	-	X optional	-

	Visit 1: Baseline (Week 0)	**Visit 2: (Week 1) Telehealth Visit**	**Visit 3: (Week 4) Telehealth or in person**	**Visit 4*: (Week 13)**	**Visit 5: (Week 14) Telehealth Visit or in person**	**Visit 6: (Week 25)**	**Visit 7**: End of Week 49**	Visit 8**: End of week 61 (+/- 7 days) Telehealth visit	Continuation Visit 9**: Up to the end of week 73 or End of Treatment	**Safety Visit*** 4 weeks after last dose of study drug. Telehealth Visit or in person**
Pill counts	-	X	X	X	-	X	X	-	X	-
Review of adverse events (AE)	-	X	X	X	-	X	X	-	X	X
Dose Increase		X	-	-	-	-	-	-	-	-
Determination to continue study drug	-	-	-	-	X	-	-	-	-	-

*After you have been on study drug for 13 weeks (visit 4), you will have tests and procedures to see if you are responding to study drug. While we check for the results of the tests, you will continue to take study drug for up to another week. Once we have the results, we will schedule a telehealth visit (Visit 5) to discuss them with you. If we find that you are responding to study drug (meaning your brain or spine MRI shows no new or larger lesions or your lesions have improved) we will give you about up to 59 more weeks of study drug at 10 mg twice a day or the dose that gives you the least side effects. If we find that study drug is not benefiting you, we will switch you to a lower dose of 5 mg twice a day for one week before stopping the study drug to prevent side effects from stopping the drug too quickly.

**Visits 6, 7, 8 and 9 will only occur if you continue therapy after end of week 13 assessment (Visit 4).

***This visit will occur 4 weeks after last dose of study drug and as needed if you have adverse events or if doctors at NIH decide to see you again. It may occur via Telephone or TeleHealth or in person in NIH. If it happens in NIH all tests/procedures are optional, except for adverse events (AE) review and collection. If you continue to have AEs during last safety visit (4 weeks after last dose), we might see you in NIH for additional unscheduled safety visits, until all AEs are resolved.

Visit 2, 5 and 8 are Telehealth Visits, you don't have to travel to NIH.
During visit 2 we will review adverse events, pill count, the dose increase and blood draw, which may be done at your local doctor's office or phlebotomy laboratory.

During visit 5 we will determine if the drug should be continued or stopped.

The following procedures may be performed on this study:

Clinical and Research Blood Draw:

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. The amount of blood we will draw is about 150ml (about 2/3 cup) per visit.

Skin Biopsies:

We will collect a total of 3-6 skin biopsies during the study. Each time we will clean your skin and then inject a local numbing medicine. This may sting a little. After we have numbed your skin, we will use a cutting device to remove a small piece of skin. The biopsies are often small enough that they do not require sutures. We will put a clean dressing on the areas and ask you to keep them dry for 48 hours at which point you can shower. You will need to clean the biopsy sites with soap and water every day after the first 48 hours and put a new bandage on to minimize the chance of infection. The skin biopsies will be used for research only.

Lumbar Puncture:

You will have a lumbar puncture (sometimes called a "spinal tap") to obtain cerebral spinal fluid (CSF) samples. We will insert a small needle into your lower back. Then we will help you either lay on your side or sit up. We will clean the lower part of your back with antiseptic, and then we 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 4 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 (LP) is complete, you will be watched for about 30 minutes. To prevent side effects, it is important that you not do any strenuous physical activity for 24 hours after the procedure. For example, you should not do any lifting, bending, doing housework and gardening, or exercising.

Brain and Spine MRIs:

An MRI makes pictures of the inside of your body using strong magnets instead of x-ray energy. At the time of each scan, you will be asked to fill out a screening form to verify that it is safe for

you to have the scan. You will also be asked to remove any metallic objects you may be wearing (for example, watches, earrings or piercings). We may ask you to change into a hospital gown.

Then you'll be asked to lie on a narrow bed that will move into the MRI scanner. Once you are comfortable, the table will be moved into the scanner (the scanner is a long, narrow tube that is open at each end). You will need to lie still on the table during the scan. The scan will take about 60-90 minutes to complete. You will hear normal "hammering" or clicking and squealing noises during the scan. We will give you earplugs or earmuffs to muffle the sound. You will be able to communicate with the technician running the scan the entire time. We will give you an emergency button to squeeze at any time if you decide you want the scan to stop.

Gadolinium-based contrast agents: During part of the MRI we will give you gadolinium, a contrast agent, through an intravenous (IV) catheter (small tube). It will be done for medical and research uses.

Genetic Testing: We will use some of your blood, skin, and spinal fluid to make RNA (also called ribonucleic acid). RNA carries the instructions from the DNA to the parts of your cells that make proteins. To look at your RNA, we may use do what is called "RNA sequencing." We will do special tests in the lab to look at the order (also called a sequence) of how your RNA is put together. This is what makes you unique.

Single-cell RNA sequencing involves analyzing the RNA of various cells one by one, which gives us information on the specific genes that are active in each cell. By doing so, we can understand how cells interact and communicate with each other.

You should know that the analyses that we do in our lab are for research purposes only. They may not be as accurate as the genetic tests that are done for routine clinical care. Because these sequences will not be used for clinical care, we do not plan on giving you the results of these research sequences.

Pill Counts

You will be asked to bring your study medication pill bottles with any remaining pills to each study visit so we can do a pill count. This helps us keep track of your medications and see if there are any missed doses.

HOW LONG WILL THE STUDY TAKE?

If you agree to take part in this study, your involvement is expected to last for approximately 17-77 weeks. Each visit will last for approximately 1- 3 days.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

You are the only patient participating in this protocol.

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

While you are on the study, you may experience side effects from tests, procedures or ruxolitinib. You should discuss any side effects with the study team and/or your regular doctor. You may have side effects that we cannot predict. If needed, we will give you medications to treat the side effects.

Risks Related to Ruxolitinib

Low Blood Counts: Ruxolitinib may cause low numbers of platelets (thrombocytopenia) which are important in blood clotting, anemia (low numbers of red blood cells), and neutropenia (low numbers of some white blood cells which fight infections). Because low white blood cell counts have been observed in patients with Degos disease, there is a chance the addition of ruxolitinib may make this worse. We will watch for this from the beginning and throughout the study.

Infection: Serious infections caused by bacteria and other types of organisms have occurred with ruxolitinib. Because you are already taking another drug eculizumab (also called by its brand name Soliris), which increases the susceptibility to infection, you may be at additional risk with this combination of medications.

TB: Tuberculosis infection has been reported in patients receiving ruxolitinib. If you are at high risk of TB (prior residence in or travel to countries with a high prevalence of tuberculosis, close contact with a person with active tuberculosis, and a history of active or latent tuberculosis where an adequate course of treatment cannot be confirmed) we will assess you for TB before we start ruxolitinib.

Progressive multifocal leukoencephalopathy (PML): PML is a serious and fatal (deadly) brain infection caused by a virus that has in rare cases happened in people taking ruxolitinib.

Herpes Zoster (shingles): Shingles has happened in people taking ruxolitinib. If you notice any symptoms (painful rash) please tell us so treatment can be started as early as possible

Hepatitis B: Ruxolinitib may increase the amount of Hepatitis B virus if you have chronic HBV infections.

Ruxolitinib Discontinuation Syndrome: Some patients stopping ruxolitinib too quickly, without a dose taper, have had one or more of the following adverse events: fever, respiratory distress, low blood pressure, small blood clots, or multi-organ failure.

Lipid Elevations: Taking ruxolitinib has caused increases in lipids including total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides.

Non-Melanoma Skin Cancers: Non-melanoma skin cancers (NMSC)s, have been reported in people taking ruxolitinib. We do not know if ruxolitinib caused these cancers. We recommend a periodic skin examination if you are at increased risk for skin cancer.

Some Side Effects have been seen with other Drugs in the Same Class as Ruxolitinib is (A JAK/STAT Inhibitor) but not with Ruxolitinib itself.

Venous Thromboembolism (blood clots in the veins): Other drugs that work in a similar way as Ruxolitinib and have been used to treat people with autoimmune diseases may cause blood clots in the leg or lung. This has not been seen with ruxolitinib, but because the drugs work in a similar way, it is possible that Ruxolitinb might also cause these blood clots. .

Secondary Malignancies (Cancers): Another drug that works in a similar way to Ruxolitinib (not ruxolitinib) increased the risk of lymphoma and other cancers in people with rheumatoid arthritis. Current or past smokers are at additional increased risk.

Major Adverse Cardiovascular Events (MACE): MACE are major side effects that include things like heart attacks and strokes or other heart problems can lead to death. Another drug that works in a similar way to Ruxolitinib has shown an increased risk of MACE, so it is possible that Ruxolitinib might also cause these side effects.

GI perforation: Treatment with another drug that works like Ruxolitib has shown to result in an increased risk of intestinal perforation (holes in the bowel). People with systemic Degos disease are already at higher risk of intestinal perforation and we do not know if the addition of ruxolitinib will increase this risk even more.

Unknown Side Effects: Ruxolitinib may involve risks that we don't currently know about. If we have any significant new findings during the study that might affect your willingness to participate, we will tell you as soon as possible.

Risks associated with procedures or tests:

Blood Draw: Blood draws may cause pain, redness, bruising or infection where we put the needle. Rarely some people faint.

Skin biopsy: Pain at the biopsy site should be minimal. Bleeding and infections are rare. Biopsy wounds heal with a very small, nearly unnoticeable scar. Sometimes a raised scar (keloid) or visible lump may result. The numbing medicine is used to reduce the pain of the biopsies; however, there is some burning pain caused by the injection of the numbing medicine. The pain may not be eliminated completely. You may have mild pain and tenderness at the biopsy site for up to 1 week after the skin biopsy. In rare cases, allergic reactions to the numbing medication have been reported. Please tell us if you ever have had an allergic reaction to any medications. It is also possible that the biopsy site can become infected and need additional treatment. If you develop signs of infection at the biopsy site such as expanding redness, swelling, or discharge, please seek medical attention and notify us.

Lumbar puncture (LP): The lumbar puncture may cause pain at the site where the needle goes into your skin, and where the spinal fluid is taken. There is a small risk of infection or bleeding.

You may get a headache after the LP. About 1 in 3 adults report a headache after an LP. To minimize the risk of a headache, the doctor will use a small needle during the procedure. The doctor may also prescribe bed rest for one or more hours after the procedure. If you get a headache, it is usually mild and can be controlled with 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 usually stops the headache.

A rare but serious complication of a LP is known as a medullary herniation, which can cause death. This can happen if the LP is done when the pressure inside your head is higher than normal (such as when a brain tumor is present),. Increased pressure inside your head is very unlikely. We will not do the LP if there are any signs that you have increased pressure inside your head. We will also not do the LP if you have a skin infection in the lower back area, or if

you have bone defects of the lower back (including severe scoliosis) which would make an LP difficult to do.

To minimize these risks, the LP will be done by a medical professional specifically trained to do this procedure.

Also see "Allergic Reaction" above for risks related to the use of lidocaine.

MRI Scans: You might be at risk for injury from the MRI magnet if they have some kinds of metal in your 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 tell us. 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.

If you are afraid of confined (small, cramped) spaces, you may become anxious during an MRI. If you have back problems, you may have back pain or discomfort from lying in the scanner.

The noise from the scanner is loud enough to damage hearing, especially if you already have hearing loss. We will give you hearing protection. If the hearing protection comes loose during the scan, you should let us know right away.

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

Gadolinium-based contrast agents: The risks of an IV catheter include bleeding, infection, or inflammation of the skin and vein. These could cause 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:

- your arm being cold during the injection,
- a metallic taste,
- headache, and
- nausea.

More severe symptoms have been reported in an extremely small number of people (fewer than 1 in 300,000 people). These symptoms include:

- 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)". NSF always involves the skin and can also involve the muscles, joints, and internal organs. NSF has resulted in a very small number of deaths. We may do a blood test of your kidney function within 30 days 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 long-term effects of the retained gadolinium are unknown. 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. We will also give you additional information called a "Medication Guide." If you ask, we will give you individual information about remaining gadolinium we see on your scans.

Genetic Testing: There are minimal risks associated with the type of RNA sequencing we will do in this protocol.

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You may not benefit from being in this study. However, the potential benefit to you might be slowing the progression of neurologic changes, symptoms and on imaging.

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

In the future, other people might benefit from this study because the knowledge we gain may help us determine a new treatment for systemic Kohlmeier-Degos disease.

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 not to enroll in this study.

- Choose to withdraw from this study. You can withdraw from the study at any time. In this case. we will keep your study results in order to properly analyze them. If you, at any time, decide to withdraw, please tell us.

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 will share all clinically relevant results with you.

EARLY WITHDRAWAL FROM THE STUDY

If new, previously undisclosed information emerges during the study that would exclude you from the study, the investigators will discuss this with you, and you may be taken off the treatment (you will stop taking ruxolitinib) and/or off the study (you will no longer participate in this study).

You can stop taking part in the study at any time.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

Will your specimens or data be saved by the study team for use in other studies?

As part of this study, we are obtaining specimens and data from you. We plan to store and use these specimens and data for studies other than the one described in this consent form that are going on right now, as well as studies that may be conducted in the future. The specimens and data will be kept in a way that we will still know that they came from you (i.e., they will be identifiable to us). If we use your identifiable specimens or data for future research, our study will be reviewed and approved by an Institutional Review Board who will make sure that we are protecting your confidentiality. These future studies might help us better understand Kohlmeier-Degos Disease 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 identifiable specimens and data to be stored and used by the study team for future studies as described above.

_____ Yes _____ No

Initial Initial

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

We may share your specimens and data with other researchers. The other researchers may be doing studies in similar areas to this study or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or at commercial entities.

One way that we may share your data is by putting it into a large database called a repository, which is a way to make it widely available to the research community. If we do place your data in a repository, it will be labeled with a code, (not with your name or other information that could be used to easily identify you). Even though it will only be labeled with a code, some types of data, in particular data about your genes (called genetic or genomic data), can be used to figure out who you are, although this is difficult to do, and we think it is unlikely to happen.

The data in the repository will only be available to qualified researchers. These researchers must receive permission before they are allowed to access the data. Before receiving the data, the researchers must promise that they will not try to figure out the identity of the research participants.

If we do share your specimens or data, we will know that the specimens and data came from you. However, the other researchers will not know that they came from you (i.e., they will be de-identified).

I give permission for my **de-identified** specimens and data to be shared with and used by other researchers for future studies.

_____ Yes _____ No

Initial Initial

In some cases, it may help other researchers to know that the specimens or data were collected from you (i.e., they will have your identifiers). If we share your identity with other researchers, their study will be reviewed and approved by an Institutional Review Board who will make sure that the study team is protecting your confidentiality.

I give permission for my **identifiable** specimens and data to be shared with and used by other researchers for future studies.

_____ Yes _____ No

Initial Initial

In addition to the planned use and sharing described above, we might remove any labels from your specimens and data that might identify you (i.e., anonymize them), and use them or share them with other researchers for future studies at the NIH or other places. When we or the other researchers use your anonymized specimens and data for these projects, there will be no way to know that they came from you. We want to make sure that you understand that this is a possibility if you participate in this study. Once we do this, we would not be able to remove your specimens or data from these studies or prevent their use in future studies because we would not be able to tell which specimens or data belong to you.

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 who 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 that no one will 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.

Can you change your mind about use and sharing for future research?

If you change your mind and do not want us to store and use your specimens and data for future studies, you should contact the study team. 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 is already complete, the information from that research may still be used. Also, if the specimens and data have been shared already, it might not be possible to withdraw them.

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

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

PAYMENT

Will you receive any type of payment for taking part in this study?

You will not receive any payment for taking part in this study.

REIMBURSEMENT

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

This study will offer a reimbursement for travel, meals, and lodging in accordance with the NHLBI travel policy.

COSTS

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.

All home doctor visits that are part of the routine management of your disease or for other health needs are your responsibility or the responsibility of your insurance company. There may be additional costs to you, including the amount of personal time it will take to come to all the study visits.

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.

No NIH investigator involved in this study receives payments or other benefits from any company whose drug, product or device is being tested.

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

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 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.

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, about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Dr. Cornelia Cudrici, cudricicd@mail.nih.gov, 240-515-5540. 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

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date