Title: A Single Arm, Open Label, Phase II Study of Ruxolitinib in Sclerotic Chronic Graft-Versus-Host Disease after Failure of Systemic Glucocorticoids

NCT Number: NCT03616184

Date of the document: 04/07/2022

ADULT CONSENT - CLINICAL BIOMEDICAL

Title of this Research Study

Invitation
You are invited to take part in this research study. You have a copy of the following, which is meant to help you decide whether or not to take part:

- Informed consent form
- "What Do I need to Know Before Being in a Research Study?"
- The Rights of Research Subjects

Why are you being asked to be in this research study?
Your doctor invited you to take part in this study because you have sclerotic chronic graft-versus-host disease (GVHD) after hematopoietic cell transplantation that is not responding to treatment.

Up to 47 people will participate in this trial at many centers across the United States. Up to 18 will be enrolled in this study at the University of Nebraska Medical Center.

If you are pregnant, nursing an infant, or plan to come to become pregnant during this study, you may not be in this study.

What is the reason for doing this research study?
Sclerotic chronic GVHD is an important complication of transplant that can cause unwanted symptoms and disability in many different parts of your body. Many times, sclerotic chronic GVHD do not respond well to initial treatments, and therefore will need to go on to additional types of chronic GVHD treatment. This research study will investigate whether a drug called ruxolitinib can effectively treat sclerotic chronic GVHD.

The study drug, ruxolitinib, has been approved by the Food and Drug Administration (FDA) to treat other blood disorders, but not sclerotic chronic GVHD. The use of ruxolitinib in patients with chronic GVHD is investigational.

What will be done during this research study?
You may be in this study for up to 24 months after study enrollment. If you decide to participate in this study, you will come to clinic for the following study visits:

Baseline Assessments:
The investigator will discuss the study with you, and ensure that you are eligible to take part. If you choose to take part in this study, you will be invited to signed this form. You will be assigned a study number which will be used to identify you throughout the study. Your medical history will be reviewed. As part of your baseline visit:

1. You will have a physical exam
2. Standard clinical laboratory blood tests will be performed. Additional tests will be performed to check your blood lipid levels and pancreatic enzymes. We will confirm that you do not have serious infectious problems including hepatitis and HIV; tests will be performed if they have not been previously done.
3. You will have an electrocardiogram (EKG) to check how your heart is doing.
4. If you are a woman of child-bearing potential, a pregnancy test will be performed.
5. Blood will be collected from you for a research blood sample for this study during this visit. These samples will be used to study how ruxolitinib affects the immune system. You will not have more than 30ml (about 2 tablespoons) of blood drawn for this research study at a single visit.
6. You will complete 2 questionnaires about your chronic GVHD and your quality of life. It will take you about 30-45 minutes to complete the questionnaires.
7. The investigator will assess your GVHD using physical examination, and digital pictures.
8. You will receive study drug

This visit will take about 2 -3 hours to complete.

Study Treatment:
Ruxolitinib (the study drug) is an oral therapy (tablet) that you will take twice a day for up to 7 months. If the drug is helping you at 6 months, you will take it up to 13 months in total. You will fill out a medication diary to track your doses.

Day 14 & Day 28 ±4 days:
The following will be performed at this visit:

- Standard clinical laboratory blood tests

This visit will take about 30-60 minutes to complete. If you complete the clinical lab tests with your primary care provider and not at the research center, you will receive a phone call from study personnel if there are abnormal results.

Month 2, 4, and 5 ±14 days:
The following will be performed at this visit:

- Standard clinical laboratory blood tests.

This visit will take about 30-60 minutes to complete. If you complete the clinical lab tests with your primary care provider and not at the research center, you will receive a phone call from study personnel if there are abnormal results.

Month 3 and 6 ±14 days:
The following will be performed at this visit:

- A history and physical exam including GVHD evaluation and digital pictures,
- Standard clinical laboratory blood, including tests for blood lipid levels and pancreatic enzymes, if needed (at month 3 visit).
- Research blood samples collected for the study
- Picking up your supply of study drug
- Filling out questionnaires about your GVHD

These visits will take about 1-2 hours to complete.

Extended Treatment:
At 6 months, if the drug is helping you, you will be followed for up to a total of 2 years (9, 12, 15, 18, 21 and 24 months ±30 days). If the drug is helping you at 6 months (that is GVHD is stable or responding), you will receive ruxolitinib for 7 to 13 months. You will come to clinic for:

- A history and physical exam including GVHD evaluation and digital pictures
- Standard clinical laboratory blood tests
- Picking up your supply of study drug (until you stop taking the study drug)
- Filling out questionnaires about your GVHD

These visits will take about 1-2 hours to complete.

Safety follow-up:
After you finish taking the study drug, you will enter the safety follow-up part of the study. This will occur 30-40 days after your last dose. You will have a history and physical exam, and standard clinical laboratory blood tests This visit will take about 30-60 minutes to complete.

Data collection from review of your medical record may continue even when you are off the study drug.

What are the possible risks of being in this research study?
While on this study, you are at risk for side effects. These side effects will vary from person to person. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death. Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs.

Ruxolitinib: The following side effects have been observed in patients who have been treated with ruxolitinib.

Common Risks (10% or more of people taking this drug report these side effects):

- Anemia (low red blood cells)
- Neutropenia (low white blood cells)
- Thrombocytopenia (low platelets)
- Bruising
- Raised ALT and AST (blood proteins that may indicate mild liver damage)
- Hypercholesterolemia (increase in cholesterol)
- Hypertriglyceridemia (increase in triglycerides)
- Dizziness
- Headache
- Urinary tract infections
- Weight Gain

Less Common Risks (1-10% of people taking this drug report these side effects):

- Gas
- Constipation
- Herpes zoster (shingles)
- Hypertension (high blood pressure)

Ruxolitinib may cause low blood cell counts (white blood cells, red blood cells and platelets). If your white blood cell count becomes low while you take the drug, this means that there may be more of a chance of getting an infection, including urinary tract infections and viral infections. You will be checked for any signs of infection before starting ruxolitinib and any serious infections should be treated before you start ruxolitinib; your physician will check you carefully for signs of infection while you are being treated.

You also may become anemic (low red blood cell count) while you take the drug, and

that may cause you to feel fatigued or short of breath. If your platelet count becomes low while you take the drug, it may lead to bleeding and/or bruising. In some people taking ruxolitinib, the decreases in blood cell counts have been severe. In most cases, low blood cell counts can be reversed by stopping the study drug temporarily or reducing the dose; you will be checked often for this side effect while on study. If your blood cell counts do not recover quickly, your study drug dose may be stopped for a longer duration to allow the blood cell counts to recover.

Uncommon Risks (1% or less of people taking this drug report these side effects):
These events are events that were uncommon, but have occurred in patient during ruxolitinib treatment are potentially serious.

Tuberculosis has occurred in a small number of patients (less than 1%) who were treated with ruxolitinib, but it is not known whether this was due to ruxolitinib, or other factors that are known to increase the risk of tuberculosis (such as diabetes, bronchitis, asthma, smoking, emphysema, or steroid use). Tell your study doctor if you have been treated for TB in the past, or have ever had a positive skin test for TB. Additionally, you should tell your study doctor immediately if you have any of the following symptoms while on the study: chronic cough with blood-tinged sputum, fever, night sweats, weight loss.

About one week following interruption or discontinuation of ruxolitinib, some patients may experience a return of symptoms (such as fatigue, bone pain, fever, itching, night sweats, weight loss, or an enlarged spleen). There have been cases of patients stopping ruxolitinib during another ongoing illness who became more severely ill, but it was not clear whether stopping therapy contributed to the patients conditions worsening.

A rare disease called progressive multifocal leukoencephalopathy (PML) has been reported during ruxolitinib treatment. PML comes from a viral infection that causes brain damage and can be fatal. It is unknown whether this was due to ruxolitinib treatment since PML has occurred in patients with blood cancers who were not treated with ruxolitinib. Tell your study doctor immediately if you have any of the following symptoms or if anyone close to you notices that you have any of these symptoms: confusion or problems thinking, loss of balance or problems walking, clumsiness, difficulty speaking, decreased strength or weakness on one side of your body, blurred and/or loss of vision.

Questionnaires: Some questions about the impact of chronic GVHD may upset you.

You may skip any question for any reason.

Blood Draw: The risks of blood draws are pain, bruising, infection, redness, and swelling at the site of the needle entry. There is a chance you may feel dizzy while your blood is being drawn. If you have severe anemia, blood collection for research may be delayed or canceled.

Reproductive Risks: It is possible that the medicines used in this study could injure a fetus if you, or your partner, becomes pregnant while taking them. You have already been told what is known about this possibility, and you are encouraged to ask further questions.

You may want to discuss this with others before you agree to take part in this study. If you wish, we will arrange for a doctor, nurse, or counselor who is not part of this study to discuss the potential risks and benefits with you and anyone else you want to have present.

Because of the potential risks, you, or your partner, must not become pregnant while you are participating in this study. Women must have a negative pregnancy test before entering the study.

If you are sexually active and can get pregnant, or can get your partner pregnant, you must use two appropriate method(s) of birth control every time you have sex, or you must not have sex.

- Condoms (male or female) with or without a spermicidal agent
- Diaphragm or cervical cap with spermicide
- IUD
- Hormonal based contraception

Because of the nature of this research, methods of natural family planning are not, by themselves, sufficiently reliable to avoid pregnancy.

You can get additional information about methods to avoid pregnancy by calling the UNMC Research Subject Advocate's Office at (402) 559-6941.

You will need to continue to avoid pregnancy for 3 months after the last dose of ruxolitinib.

By signing this and being in the study, you are agreeing to not get pregnant while you are on the study and for 3 months after. Should you become pregnant while on this

study, you should immediately notify the study personnel. The investigator will assist you in finding appropriate medical care. The investigator also may ask to be allowed to continue getting information about your pregnancy. You can refuse to provide this information.

Risks to breast-fed children: It is possible that the study medication could be present in breast milk and injure a breastfed baby. Women should not breast-feed a baby while on this study. Breast-feeding mothers must stop breast-feeding to take part in this study.

What are the possible benefits to you?
The major potential benefit is that this study treatment could improve your sclerotic chronic GVHD. You may not get any benefit from being in this research study. We do not know if this study will help patients directly.

What are the possible benefits to other people?
The information learned from this study will help physicians learn more about ruxolitinib as a treatment for GVHD. The research blood tests may also provide information regarding the effect of GVHD and ruxolitinib on immune system. This information may someday be of benefit to future patients.

What are the alternatives to being in this research study?
Instead of being in this research study, you can choose not to participate. If you do not join this study, you have other choices for treatment. One FDA approved treatment for your condition is ibrutinib.

Before you decide to take part in this study, your study doctor will talk with you about other options available to you, which may include other medications, treatments, or dose changes in your current medications. The investigators will discuss with you the risks and benefits of each of the alternatives described above.

What will being in this research study cost you?
You or your insurance company will not be billed for tests and procedures done specifically for this study (i.e., extra blood drawn for research, pregnancy tests, questionnaires). Ruxolitinib will be provided free of charge from Incyte Corporation.

There are some extra costs for being in this study. You or your insurer will have to pay these costs. Some insurers will not pay for research. Check with your insurer before you join this study.

Whether you are in the study or not, you or your insurance company will be responsible for medications, tests, clinic and hospital visits as part of your routine care as a transplant recipient.

You will be responsible for any applicable insurance deductibles and co-payments. If you wish to speak with a financial counselor about your insurance coverage and benefits, let the investigator or other study personnel know. A contact for personal assistance will be made available for you.

Will you be paid for being in this research study?
You will not be paid to be in this research study.

Who is paying for this research?
This research is being paid for by grant funds from Incyte Corporation. The Institution receives money from Incyte Corporation to conduct this study.

Dr. Vijaya Bhatt, the Principal Investigator of this study, receives money providing consulting services to Incyte Corporation.

What should you do if you are injured or have a medical problem during this research study?
Your welfare is the main concern of every member of the research team. If you are injured or have a medical problem as a direct result of being in this study, you should immediately contact one of the people listed at the end of this consent form. Emergency medical treatment for this injury or problem will be available at the Nebraska Medical Center. If there is not sufficient time, you should seek care from a local health care provider.

The Institution has no plans to pay for any required treatment or provide other compensation. If you have insurance, your insurance company may or may not pay the costs of medical treatment. If you do not have insurance, or if your insurance company refuses to pay, you will be expected to pay for the medical treatment.

Agreeing to this does not mean you have given up any of your legal rights.

How will information about you be protected?
You have rights regarding the protection and privacy of your medical information collected before and during this research. This medical information is called "protected health information" (PHI). PHI used in this study may include your medical record number, address, birth date, medical history, the results of physical exams,

blood tests, x-rays as well as the results of other diagnostic medical or research procedures. Only the minimum amount of PHI will be collected for this research. Your research and medical records will be maintained in a secure manner.

Who will have access to information about you?
By signing this consent form, you are allowing the research team to have access to your PHI. The research team includes the investigators listed on this consent form and other personnel involved in this specific study at the Institution.

Your PHI will be used only for the purpose(s) described in the section "What is the reason for doing this research study?"

You are also allowing the research team to share your PHI, as necessary, with other people or groups listed below:

- The UNMC Institutional Review Board (IRB)
- Institutional officials designated by the UNMC IRB
- Federal law requires that your information may be shared with these groups:
    - The HHS Office of Human Research Protections (OHRP)
    - The Food and Drug Administration (FDA)
    - National Institutes of Health (NIH)
- The HIPAA Privacy Rule requires the following groups to protect your PHI
    - Your health insurance company
    - The Fred & Pamela Buffett Cancer Center Scientific Review Committee (SRC).

Your PHI may also be shared with the following groups. However, these organization(s) do not have the same obligation to protect your PHI:

- Incyte Corporation and Novartis International Pharmaceutical Ltd., provides funds the Institution to conduct this research
- Data and Safety Monitoring Committee (DSMC)
- The National Cancer Institute's (NCI) Clinical Trial Reporting Program

Your information may be kept and used indefinitely.

You may cancel your authorization for further collection of PHI for use in this research at any time by contacting the principal investigator in writing. However, the PHI which is included in the research data obtained to date may still be used. If you cancel this authorization, you will no longer be able to participate in this research.

How will results of the research be made available to you during and after the

study is finished?
In most cases, the results of the research can be made available to you when the study is completed, and all the results are analyzed by the investigator or the sponsor of the research. The information from this study may be published in scientific journals or presented at scientific meetings, but your identity will be kept strictly confidential.

If you want the results of the study, contact the Principal Investigator at the phone number given at the end of this form or by writing to the Principal Investigator at the following address:

Vijaya Bhatt, MBBS
9876840 Nebraska Medical Center, Omaha, NE 68198-6840

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

What will happen if you decide not to be in this research study?
You can decide not to be in this research study. Deciding not to be in this research will not affect your medical care or your relationship with the investigator or the Institution. Your doctor will still take care of you and you will not lose any benefits to which you are entitled.

What will happen if you decide to stop participating once you start?
You can stop participating in this research (withdraw) at any time by contacting the Principal Investigator or any of the research staff.

Deciding to withdraw will otherwise not affect your care or your relationship with the investigator or this institution. You will not lose any benefits to which you are entitled.

For your safety, please talk to the research team before you stop taking any study drugs or stop other related procedures. They will advise you how to withdraw safely. If you withdraw you may be asked to undergo some additional tests. You do NOT have to agree to do these tests.

You may be taken off the study if you do not follow instructions of the investigator or the research team.

You may also be taken off the study if

- your GVHD progresses, resulting in starting of a new systemic immunosuppressive medication
- you develop an adverse reaction that requires you to discontinue the study drug
- you develop an allergic reaction or sever intolerance to the study drug
- you develop other medical problems that make continuing the study could cause you harm
- you choose to discontinue the study drug

Any research data obtained to date may still be used in the research.

Will you be given any important information during the study?
You will be informed promptly if the research team gets any new information during this research study that may affect whether you would want to continue being in the study.

What should you do if you have any questions about the study?
You have been given a copy of "What Do I Need to Know Before Being in a Research Study?" If you have any questions at any time about this study, you should contact the Principal Investigator or any of the study personnel listed on this consent form or any other documents that you have been given.

What are your rights as a research participant?
You have rights as a research subject. These rights have been explained in this consent form and in The Rights of Research Subjects that you have been given. If you have any questions concerning your rights, or want to discuss problems, concerns, obtain information or offer input, or make a complaint about the research, you can contact any of the following:

- The investigator or other study personnel
- Institutional Review Board (IRB)
    - Telephone: (402) 559-6463.
    - Email: IRBORA@unmc.edu
    - Mail: UNMC Institutional Review Board, 987830 Nebraska Medical Center, Omaha, NE 68198-7830
- Research Subject Advocate
    - Telephone: (402) 559-6941
    - Email: unmcrsa@unmc.edu

Optional Long-term Storage of Leftover Blood Samples

You may take part in these additional studies if you want to. You can say "yes" or "no" to this option. You can still be a part of the main study even if you say 'no' to taking part in this additional study. **Please mark your choice with your initials.**

The researchers doing this study are interested in doing additional research now or in the future on the samples collected from you to better understand the nature of GVHD and how patients respond to treatment. Rapid advances in technology make it impossible to predict what new tests or studies may be possible in the future.

The required collection of these research blood samples will be before you begin treatment and at months 3 and 6. The samples will not be sold. If you allow, we will store leftover samples for future use.

The samples will be kept until they are used up or destroyed.

Reports about any research tests done with your samples will not be given to you or your oncologist, or family doctor. These reports will not be put in your medical records.

Confidentiality of Samples
To protect your identity, the information that will be on your blood samples will be limited to the participant code. The samples may possibly be traced back to you, but we will take steps to protect your confidentiality.

Withdrawal of Required Samples
If you no longer want your samples to be used in this research, you should tell the investigator. The investigator will ensure the samples are destroyed. If tests have already been done on your sample(s) it will not be possible to withdraw those results. However, no further testing will be done.

This research may not benefit you, but may help people in the future who have the same kind of cancer as you have. You can indicate your wish to participate in this additional research, and have your samples stored by the University of Nebraska Medicine designated central for future extended research purposes when signing this consent form. You may decide not to participate in the "optional" study and still participate in this main study.

_____ You agree to allow storage and use of blood samples taken from you for extended research (optional).

_____ You do not agree to storage and use of blood samples to be stored for extended research (optional).

Documentation of informed consent
You are freely making a decision whether to be in this research study. Signing this form means that:

- You have read and understood this consent form.
- You have had the consent form explained to you.
- You have been given a copy of The Rights of Research Subjects
- You have had your questions answered.
- You have decided to be in the research study.
- If you have any questions during the study, you have been directed to talk to one of the investigators listed below on this consent form.
- You will be given a signed and dated copy of this consent form to keep.

Name of Subject _____

Signature of Subject _____

Date _____

My signature certifies that all the elements of informed consent described on this consent form have been explained fully to the subject. In my judgment, the subject possesses the legal capacity to give informed consent to participate in this research and is voluntarily and knowingly giving informed consent to participate.

Name of Person Obtaining Consent _____

Signature of Person Obtaining Consent _____

Date _____

Authorized Study Personnel
Principal
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