PRINCIPAL INVESTIGATOR: [redacted]

STUDY TITLE: Phase II Study of Topical Ruxolitinib for Cutaneous Chronic Graft versus Host Disease (cGVHD)

STUDY SITE: National Institutes of Health (NIH)

Cohort: *Assent*

Assent Version: 01/25/2021

We would like to invite you to take part in a research study at the National Institutes of Health (NIH). Before you decide about taking part in the study, we want you to know why we are doing the study and if it will help you. We also want you to know about any risks (something that may be unpleasant) and what you will have to do as part of this study. You can only be in the study if you and your parent(s) agree.

This form gives you information about the study. Your doctor will talk to you about the study and answer questions you have. If you would like to take part in this study, we will ask you to sign this form to show that you understand this study. We will give you a copy of this form to keep. It is important that you know:

- You do not have to join the study.
- You may change your mind and drop out of the study at any time.

If we make important changes to the study we will tell you about it and make sure you still want to be in the study.

WHY IS THIS STUDY BEING DONE?

We are asking you to take part in a research study because we are trying to learn more about Chronic graft versus host disease (cGVHD), a condition you have. cGVHD happens in about half of patients that have had a hematopoietic cell transplant using donor cells. Because the immune cells given to you come from another person (donor), they may not recognize the tissues in your body and attack your body causing damage. cGVHD can affect different parts of the body such as the lungs, stomach, intestines, liver, and connective tissue in the skin and joints. This study looks at cGVHD in the skin.

Ruxolitinib is a medicine that works by blocking a group of proteins in your cells called Janus kinases, or JAKs. JAKs help cells respond to stimulation, which affects things like growth and how your immune system works. JAKs may send too many uninterrupted signals to cells, so cells do not behave normally. We believe these JAK proteins play a role in cGVHD. By blocking JAKs, Ruxolitinib may stop the wrong signals from going out so cells function properly. We want to learn if the cream form of Ruxolitinib will improve cGVHD in the skin.

WHAT WILL I BE ASKED TO DO? WHAT ARE MY REQUIREMENTS?

Screening

If you want to be in this study, then first we have to make sure it is safe for you to join. This is called screening.

We will talk with you and your parents or guardians about your health and how you feel. Then we will give you a checkup, take some blood from your arm with a needle to make sure you do not have a serious infection and that your liver and kidneys are working well. We can apply numbing medicine on your arm before we draw blood to help with pain.

We will also test your blood for the virus that causes AIDS. This is called an HIV test. We will share the results of the HIV test with you and your parents or guardians. You cannot be in this study if you have HIV.

Return of pregnancy results:

At each visit, we will do a pregnancy test for all females. It is very important that you are not pregnant while on the study because the treatment could hurt the baby. If you get pregnant during the study or you think that you may be pregnant, you must tell your doctor immediately. If the pregnancy test is positive, we will first tell you privately. If you would like, we can help you talk to your parents about the result. If you become pregnant while on the study, you will be taken off of this treatment immediately. If you do not want a pregnancy test, then you cannot participate in this study.

Birth Control

If you are a female who is breast feeding or pregnant, you may not take part in the study because we don't know how this medicine would affect your baby or your unborn child. If you are a female who can become pregnant, or are the partner of a female who can become pregnant, you will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 1 month after you finish study treatment. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at immediately. If you are a female who becomes pregnant while taking the study cream, you will have to stop taking the medication and will be taken off study. Effective forms of birth control include:

- abstinence
- intrauterine device (IUD)
- hormonal [birth control pills, injections, or implants]
- tubal ligation
- vasectomy

We will need to take a small piece of your skin, called a skin biopsy, and test it to make sure you have cGVHD if you have not had this done within the past 3 months.

During the study

If you are eligible and decide to be in this study you will receive both the topical ruxolitinib 1.5% cream and a placebo (inactive) cream to apply to two separate areas of disease (for example, an area on your right arm and an area on your left arm). Neither you nor your doctor will know which tube of medicine contains the ruxolitinib 1.5% cream and which tube contains the placebo cream. Your study doctor will choose the two separate areas of cGVHD on your body to be treated. You or your parent/guardian will apply the creams to each site twice a day for 6 weeks, as long as you do not experience serious side effects. You may have up to four visits at the NIH. Below is what will happen at each visit.

Visit 1: Baseline visit

- You will have a physical exam (includes temperature, height, weight, respiratory rate, heart rate and blood pressure), and the doctors will ask questions about your past medical history and review the medicines you are taking.
- The doctor will examine of all the areas of your skin that have cGVHD and will choose two sites that will be treated with the study creams. Detailed measurements of the two sites will include the physician measuring the sites with a ruler or caliper, tracing of the sites with transparency paper, taking photographs of the chosen sites and the physician will complete the Physician Global Assessment Form.
- Total Body Photographs (Optional)-We will take pictures of your entire body wearing only underwear. The study doctor may ask to have these done and will discuss this with you.
- Questionnaires (Required)-
    - Visual Analog Scales: you will be asked to complete visual scales of how bad your symptoms of cGVHD are for EACH separate site chosen to receive study medication. It will take approximately 10 minutes to complete all the scales.
- Safety blood tests: we will draw 1TBS of blood to determine if your bone marrow, liver and kidneys are working properly and a blood pregnancy test if you are a female who can become pregnant.
- You and your parent/guardian will be shown how to apply the study creams and will be asked to record each application on a daily diary.

Visit 2: You will return to the NIH 2 weeks after starting the study creams and will have:

- A physical exam (includes temperature, height, weight, respiratory rate, heart rate and blood pressure), and the doctors will ask questions about how you are feeling and review the medicines you are taking.
- The doctor will examine of all the areas of your skin that have cGVHD and will obtain detailed measurements of the two sites that are being treated including the

measuring the sites with a ruler or caliper, tracing of the sites with transparency paper, taking photographs of the chosen sites and the physician will complete the Physician Global Assessment Form.

- You will be asked to complete the Visual Analog Scales
- Safety blood tests to determine if your bone marrow, liver and kidneys are working properly including a blood pregnancy test if you are a female who can become pregnant.
- Review of study medication diary
- We will need to take 1TBS of blood at 4 different times to see if we can measure Ruxolitinib in your blood. These tests are called "PK tests." We will use a needle to put a small thin tube into your arm. This is called an "IV line." We will draw the blood samples through the IV line, so you will not need to have a needle stick each time we draw your blood.

Visit 3: At 4 weeks, you have the option of coming to NIH for a visit or having a study team member call you at home to see how you are doing. If you decide to come to the NIH you will have:

- A physical exam (includes temperature, height, weight, respiratory rate, heart rate and blood pressure), and the doctors will ask questions about how you are feeling and review the medicines you are taking.
- The doctor will examine of all the areas of your skin that have cGVHD and will obtain detailed measurements of the two sites that are being treated including the measuring the sites with a ruler or caliper, tracing of the sites with transparency paper, taking photographs of the chosen sites and the physician will complete the Physician Global Assessment Form.
- You will be asked to complete the Visual Analog Scales
- Review of study medication diary
- Safety blood tests to determine if your bone marrow, liver and kidneys are working properly including a blood pregnancy test if you are a female who can become pregnant.

Visit 4: At 6 weeks, you will return to NIH for a final evaluation to see how your skin responded to the topical creams. You will stop using the creams at this visit. At this visit you will have:

- A physical exam (includes temperature, height, weight, respiratory rate, heart rate and blood pressure), and the doctors will ask questions about how you are feeling and review the medicines are taking.

- The doctor will examine of all the areas of your skin that have cGVHD and will obtain detailed measurements of the two sites that are being treated including the measuring the sites with a ruler or caliper, tracing of the sites with transparency paper, taking photographs of the target sites and the physician will complete the Physician Global Assessment Form.
- You will be asked to complete the Visual Analog Scales
- Review of study medication diary
- Total Body Photographs (Optional)
- Safety blood tests: we will draw 1TBS of blood to determine if your bone marrow, liver and kidneys are working properly including a blood pregnancy test for females who can become pregnant.
- Research Skin Biopsy (Optional) - If you agree, the study physician will ask to obtain a skin biopsy from each treated site (2 total) at the week 6 visit to compare changes in the skin cells. If you agree to the skin biopsies you will be asked to sign a separate consent form at the time of the procedure.

Follow Up Phone Call:

A study team member will call you or your parent/guardian at home approximately 4 weeks after you stop using the creams to see how you are doing. After this phone call, your participation in this study will end.

Risks and Complications:

Risks related to the 1.5 % ruxolitinib study cream:

The ruxolitinib cream has been tested in over 2350 patients with different skin diseases. Topical ruxolitinib has so far been given to 67 children ages 2-17 without serious side effects. In studies of ruxolitinib given by mouth to young rats, some had changes in their bones. The doses given to the young rats were much higher than the dose applied to the skin in this study.

Side effects that were considered possibly related to the ruxolitinib cream were considered mild to moderate and went away without the need for other treatment. There may be side effects the doctors do not know about so it is important for you to tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.

The chart below shows the side effects that have been seen with the ruxolitinib cream.

Likely	Less Likely	Rare but Serious
• Irritation at the site of application • Itching	• Decrease in the number of white blood cells that help fight infection	• Elevation of blood enzymes that indicate injury to the liver

• Numbness or decreased sensation in area treated • Increased sensitivity to artificial and natural sunlight • Runny nose • Upper respiratory infection, • Headache • Acne	• Increase in the number of immature red blood cells • Diarrhea • Sinusitis	• Skin and other infections

Blood Draw: This might be painful and can leave a bruise or scar. Very rarely it might cause an infection. Sometimes people feel dizzy or faint. Numbing medicine can be applied before the blood draw to help with the pain.

Skin Biopsy: We will apply numbing cream to the area being biopsied to reduce pain. You may have pain, swelling or tenderness at the biopsy site. You may need one or two stiches to close the cut in your skin. This may leave a scar. Sometimes the scar does not fade. The biopsy site could also become infected. The study team will give you instructions on how to care for the biopsy site.

BENEFITS:

People may also have good things happen to them when they are in research studies.

Using the ruxolitinib cream might help your areas of cGVHD feel and look better or it might not. We will not know until we try it.

If you join this study, then you might help us learn more about cGVHD of the skin that could help others in the future.

Can I refuse to be in the study?

Please talk to your parents about this before you decide if you want to be in this research study. We will also ask your parents to give their permission for you to be in this study. But even if your parents say "yes," you can still decide not to be in this research study.

If you don't want to be in this study, you don't have to.

YOU MAY STOP BEING IN THIS ANY TIME

Remember, being in this study is up to you and no one will be upset if you don't want to take part in this study or even if you change your mind later and want to stop.

RE-CONSENTING

If you turn 18 while you are enrolled in this study, we will discuss if you want to continue participating in the study and you will sign a consent form (you will no longer require your parent's signature).

YOU CAN ASK ANY QUESTIONS THAT YOU HAVE ABOUT THE STUDY.

You may call me at any time to ask questions about your disease and treatment.

Putting your name at the bottom means that you have decided to be in this study. You and your parents will be given a copy of this form after you have signed it.

I have had this study explained to me in a way that I understand, I have been given the opportunity to discuss it, and I have had the chance to ask questions. I agree to take part in this study.

Assent of Participant:

Signature of Participant	Print Name of Participant	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date