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Fred Hutchinson Cancer Center
University of Washington Medical Center

Consent to take part in a research study:

Peritransplant Ruxolitinib for Patients with Primary and Secondary Myelofibrosis

[**Short title: Peritransplant Myelofibrosis**]

Part 2 of the study: Ruxolitinib and Transplant

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If you are serving as a legally authorized representative in this study, the terms "participant", "you", and "your" refer to the person for whom you are providing consent.

Important things to know about this study.

You are invited to participate in a research study. The purpose of this research is to find out if ruxolitinib, when given prior to but then continued during and following transplant, decreases the rate of graft versus host disease (GVHD) and improves post-transplant outcomes in patients with myelofibrosis.

The study involves taking ruxolitinib before and after the transplant for both continued treatment of your myelofibrosis and the potential benefit of prevention of graft versus host disease, a complication that occurs when the donor cells recognize the patient's body as foreign and attack it.

You do not have to join this study. We will give you details about the purposes, procedures, risks and possible benefits related to this study. We will explain other choices that you have. We will also give you any other information that you need in order to make an informed decision about joining this study.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

We invite you to join this research study.

We invite you to join this research study because you have myelofibrosis and you are going to have a bone marrow, blood stem cells, or cord blood transplantation. Between 45 – 60 people will join this study.

Research is not the same as treatment or medical care. The purpose of a research study is to answer scientific questions.

You do not have to be in the study. You are free to say "yes" or "no", or to drop out after joining. If you say "no," you would have no penalty or loss of benefits. Whatever you decide, your regular medical care would not change.

Why are we doing this study?

Transplantation is standard treatment for patients with myelofibrosis in many transplant hospitals around the world. Previous experience with stem cell transplantation treatment for myelofibrosis, has led to extended disease-free survival or cure for some patients. Patients who have symptoms of myelofibrosis, such as big spleens, weight loss and fatigue often do worse with transplant than patients without these symptoms.

We are studying ruxolitinib (trade name: Jakafi). While most adult patients with advanced stage myelofibrosis receive ruxolitinib as part of standard of care, we are doing this study to look specifically at the benefits in giving ruxolitinib prior to and following transplant. In this research study, we want to learn what effects, good or bad, ruxolitinib has on people with myelofibrosis. If you join this study, we would give you ruxolitinib and watch carefully for any side effects.

A recent study done at the Fred Hutch looked at patients who received ruxolitinib prior to transplant and showed that these patients had improved post-transplant outcomes compared to previous patients who had a transplant before ruxolitinib was available. However, many of these patients had graft versus host disease as a complication of their transplant.

The purpose of this study is to find out if ruxolitinib, when given prior to but then continued during and following transplant, decreases the rate of graft versus host disease and improves post-transplant outcomes in patients with myelofibrosis. We believe this is possible based on a small study done in Europe, which suggested a decreased rate of graft versus host disease in myelofibrosis patients who continued to receive ruxolitinib during and following transplant. In this study the investigators did not see an increased risk of graft failure.

What tests, procedures, and treatments are done in this study?

If you join this study, we will perform the following tests, treatments and procedures. Many of these tests, treatments and procedures are part of your regular transplant care. These procedures are summarized in a table on page 5

- Blood and marrow samples (additional samples will be collected for research only at timepoints where blood and marrow are being collected for your regular care)
- Heme gene panel and driver mutation analysis (myelofibrosis mutations).
- Imaging for spleen assessment
- Ruxolitinib (continued following transplant)
- Busulfan (high intensity arm)
- Cyclophosphamide (high intensity arm)
- Fludarabine (reduced intensity arm)
- Melphalan (reduced intensity arm)
- Total Body Irradiation (Cord blood patients only)
- Tacrolimus
- Mycophenolate mofetil (MMF) (Cord blood patients only)
- Methotrexate (matched sibling and unrelated transplant recipients only)
- Stem cell infusion and transplant

Ruxolitinib therapy

At least eight weeks ago, you began treatment with a ruxolitinib for the treatment of your myelofibrosis. In this study you will continue ruxolitinib through the transplant for both your myelofibrosis and the potential benefit of prevention of graft versus host disease (GVHD), a complication that occurs when the donor cells recognize the patient's body as foreign and attack it. The ruxolitinib will be tapered to a dose of 5mg twice a day prior to the transplant until your transplant cells engraft. If your blood counts are stable, the ruxolitinib may be increased to a maximum dose of 10mg twice a day or kept at 5mg twice a day at the discretion of your doctor and then held at that dose until 1 month after tacrolimus is discontinued. Then it will be tapered and stopped approximately 9-12 months after transplant.

If you join this study, we will be looking at your past medical records from when you were first diagnosed with myelofibrosis, when you were started on ruxolitinib and your response to it. We will collect data from these medical records for our research study forms and our research database.

Conditioning regimen (pre-transplant chemotherapy and radiation)

Seven or eight days before the transplant, you will be given chemotherapy. You will need a central venous catheter for transplant, so if you do not already have one, one will be placed.

There are two main types of preparative (or conditioning) regimens.

- Reduced intensity regimens: These are also called non-myeloablative regimens. These regimens use relatively low doses of chemotherapy with or without radiation. This option may be helpful for patients with health conditions who are not able to have very strong chemotherapy.

- High intensity regimens: These are also called myeloablative regimens. These regimens use high doses of chemotherapy and sometimes radiation.

If you are receiving reduced intensity conditioning, you will be given fludarabine and melphalan. If you're getting a cord blood donor transplant, you will also be given total body irradiation. If you are receiving high-dose conditioning, you will be given cyclophosphamide, and busulfan. If you are receiving a cord transplant, you will also get fludarabine. Your study doctor will recommend which conditioning is appropriate for you. The intent is to help kill cancer cells and to prepare your body for the stem cells by suppressing your immune system.

Transplant Day (Bone marrow, blood stem cell, or cord blood infusion/transplant)

On day 0, the transplant day, the marrow, blood stem cells, or cord blood stem cells are given through your existing central venous catheter. The infusion of these cells may take 1 to 4 hours and feels like getting a blood transfusion.

With any source of stem cells every possible effort is made to obtain the optimum number of stem cells. If you receive cord blood stem cells, and the cord blood units contain more stem cells than required by our rules, up to 5% of the cord blood may be withheld for research purposes. These cells will be used in studies to help understand how these stem cells work in the patient and how they develop into a new immune system for you. We will also retain some cells from the marrow or blood collection from unrelated donors and use them for you after transplantation, if necessary.

High intensity conditioning				**Reduced intensity conditioning**			
Day	**Conditioning**	**Other**		**Day**	**Conditioning**	**Other**	
8 days prior to transplant	Fludarabine *			6 days prior to transplant	Fludarabine		
7 days prior to transplant	Fludarabine * Cyclophosphamide	Mesna		5 days prior to transplant	Fludarabine		
6 days prior to transplant	Fludarabine * Cyclophosphamide	Mesna Dilantin		4 days prior to transplant	Fludarabine		
5 days prior to transplant	Targeted busulfan			3 days prior to transplant	Fludarabine Melphalan		
4 days prior to transplant	Targeted busulfan			2 days prior to transplant	Fludarabine Melphalan		
3 days prior to transplant	Targeted busulfan			1 day prior to transplant	TBI *		
2 days prior to transplant	Targeted busulfan			Day 0 transplant	Transplant/infusion type		
					Cord blood	Peripheral blood	Bone marrow
1 day prior to transplant	Rest						
Day 0 transplant	Transplant/infusion type						
	Cord blood	Peripheral blood	Bone marrow				

*Cord blood recipients only ** Cord blood recipients only

Immunosuppression Therapy

As part of the transplant procedure, you will be given two drugs in addition to the ruxolitinib to reduce the risk of GVHD. The drugs will be given to you through your central venous catheter. Depending on how long you need to take each drug, the drugs may later be given to you in the form of a pill or liquid when you can take medicines by mouth. If you develop GVHD, you may take these medications for longer or receive additional medications to help treat it.

- Tacrolimus: This drug will be started one day before the transplant for patients receiving stem cells from related or unrelated donors. For patients receiving umbilical cord blood, tacrolimus will be started 3 days before the transplant. For all patients, tacrolimus will be continued for approximately 180 days after transplant.

- Methotrexate: This drug will be given on Days 1, 3, 6, and 11 after the transplant in patients receiving matched sibling or matched unrelated donor transplant.

- Mycophenolate mofetil (MMF): This study will be started on the day of the transplant in patients undergoing cord blood transplant and will be continued for approximately 40 days after the transplant.

If you are receiving a cord blood transplant, you will be given filgrastim (G-CSF or Neupogen) by injection beginning on Day 1 after your transplant. G-CSF signals the bone marrow to make white blood cells, which are needed to fight and prevent infections. You will continue to receive it daily until your white blood cell count recovers.

Post-Transplant Care at the Fred Hutchinson Cancer Center

Initially you will likely be admitted to the University of Washington Medical Center for your chemotherapy and cell infusion. After you are discharged, an outpatient transplant team will then follow you until Day 100. In order to evaluate how your new blood cells are developing and how your immune system is recovering after the transplant, you will have blood drawn and bone marrow biopsies at specific time points. Per standard practice your blood will be drawn daily until your counts recover and then twice weekly until Day 100. Blood and bone marrow studies will be done to check for presence of disease as well as presence of donor cells (chimerism tests) around Day 28 (reduced intensity only), Day 80, and at 1 year after your transplant. Spleen imaging will be performed at Day 100 post-transplant. GVHD assessment will be performed weekly by clinical exam. Evaluation by biopsies is not required for the study but may be determined as necessary by your treating physician.

Extra blood (up to 2 tablespoons) and bone marrow (up to 1 teaspoon) samples for research purposes will be collected before you undergo transplant and at day 28 (blood), between day 80-100. These research samples may be tested fresh or kept frozen for later use. The purpose of these research samples is to look for genetic mutations, which may have caused your disease and see how long they last for in your blood after the transplant. We will also look at markers of inflammation, which may have caused your symptoms and see how having markers of inflammation is associated with the gene mutations and GVHD.

After You Return Home

You will be discharged from the transplant team around day 100 when you are ready to be cared for by your home oncologist. Initially, it will be necessary for you to have frequent visits, and then at specific times as determined by your physician. Your physician will make assessments of your GVHD regularly as you taper your immune suppression drugs.

Extra blood and marrow studies will be requested at the 6-month time point and yearly from years 2 to 5 if you have persistent fibrosis or markers of disease. Spleen imaging will also be requested at 1 year. If you return to Seattle we will collect samples and do imaging at the Fred Hutchinson Cancer Center. If you are not in Seattle, you may have your samples collected and imaging done at home and we will request that the results be sent to our research team.

How long would you stay in this study?

If you join this study, you would stay in this study for about five years. After you have recovered from any immediate transplant related complications, follow-up will be

routine, but we will continue to collect data on how your marrow is functioning at these follow-up visits.

Doctors could take you out of this study at any time. This would happen if:

- They think it is in your best interest not to continue in the study.
- You are not able or willing to follow study procedures.
- The whole study is stopped.

If you withdraw from the study for any reason, previously collected information would remain in the study records and would be included in the analysis of results. This information could not be removed from the study records.

We would like to do long-term follow-up

Long-term follow-up means keeping track of someone's medical condition for a long time. Long-term follow-up means keeping track of your medical condition for the rest of your life to look at the long-term effects of the study. You will be asked to sign another consent form to allow Fred Hutchinson Cancer Center to keep getting information from your referring physician and sending you annual questionnaires about your health after you finish this study. This is done by the Long-Term Follow-Up Department, but some of the information will also be used for this study.

You do not have to be in the long-term follow-up program. You can say yes or no. Either way, you can still join this study.

What are the side effects (risks)?

In this part of the consent form, we describe the side effects we expect from the tests and treatments in this study. Ruxolitinib could cause side effects we do not know about yet. We carefully watch everyone in the study for side effects.

If you join this study, we would tell you if we discover new side effects that could affect you.

This form lists side effects of *individual* drugs. Other side effects could occur when we use these drugs *together*.

Side effects may be mild or very serious. Medicines could be given to help lessen side effects. Many side effects go away soon after you stop taking ruxolitinib. In some cases, side effects can last a long time or never go away. There also is a risk of death.

Ruxolitinib

Ruxolitinib has been studied in over 650 patients with myelofibrosis and over 40 patients with rheumatoid arthritis and the following risks have been observed:

Likely Side Effects (over 10%)	Less Likely Side Effects (3-9%)	Rare Side Effects (under 2%)
• Diarrhea	• Fatigue	• Urinary tract infection

• Nausea • Mild to moderately low blood cell counts (red blood cells (anemia) and platelets) • Shortness of breath • Swelling of the hands or feet • Feeling hot • Headache • Increased risk of bruising and bleeding • Weight gain • Heart murmur • Changes in blood pressure	• Vomiting • Low white blood cell count • Increased risk of infection • Low to moderate grade fever • Pneumonia • Bronchitis • Sleep disturbances • Pain in the arms or legs • Itchiness • Rash (viral skin infections, herpes zoster or shingles)	• Inflammation of the bowel • Gastrointestinal bleeding • Gas • High potassium count • Low levels of sodium • High cholesterol • Abdominal pain • Fainting • Neck ache • Infection or pain in joints • Severe and life-threatening form of inflammation of the pancreas • Bone marrow suppression • Significantly low red blood cells, platelets, and ANC (a type of white blood cell) • Intracerebral hemorrhage (bleeding) • Upper respiratory infection • High-grade fever • Sore throat • Low oxygen level • Inflammation of the lungs • Weakness • Anxiety • Acute response to drug withdrawal • Depression • Cardiomyopathy (weakening and enlargement of the heart muscle) • Heart failure • Acute myocardial infarction • Liver toxicity • Necrotizing fasciitis (rare infection of the deeper layers of skin and tissues underneath the skin) • Blurred vision/vision loss • Necrosis of talus bone (located in the top of the foot joining ankle)

Tuberculosis has occurred in a small number of patients with myelofibrosis who were treated with ruxolitinib, but it is not known whether this was due to myelofibrosis, ruxolitinib, or other factors that are known to increase the risk of tuberculosis (such as diabetes, bronchitis, asthma, smoking, emphysema, or steroid use).

A rare disease called progressive multifocal leukoencephalopathy (PML) has been reported during ruxolitinib treatment for myelofibrosis. 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, including myelofibrosis, 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.

Tumor lysis syndrome, a potentially serious complication of cancer treatment has also been reported rarely during treatment with ruxolitinib. Tumor lysis syndrome happens when large numbers of cancer cells are killed rapidly. Killing cancer cells quickly can lead to the release of harmful byproducts in the body's circulation system. Doctors might suspect tumor lysis syndrome when blood tests show there is a very rapid increase in uric acid (hyperuricemia), potassium (hyperkalemia), phosphorus (hyperphosphatemia), or a rapid decrease in calcium (hypocalcemia), or there are indications of acute renal failure (decreased urine output).

Some patients receiving ruxolitinib have been diagnosed with second cancers including lymphoma. It is not known whether this is related to ruxolitinib or is related to other factors, in particular the patient's genes.

There may be risks associated with sudden discontinuation of the study medication. Patients who have symptomatic heart or lung disease might experience serious and life-threatening worsening of their heart or lung condition when the study drug is stopped. It is important that you let your doctor know about any heart or lung problems prior to starting the study. If you stop taking your medication and develop worsening of your symptoms, tell your doctor right away. Other risks that might be related to discontinuation include anxiety, insomnia, weakness, recurrence of the signs and symptoms of your disease or your spleen growing back to the size it was when you started the study medication. You should tell the study doctor if you experience any of these symptoms when you stop taking ruxolitinib.

Since the study drug may have interactions with other medications, your physician may advise you not to take certain other drugs while you are on this protocol. Please check with your physician before starting any new medications or if you stop any medications.

Among patients with existing cardiac or heart problems, there have been reports of patients who experienced worsening heart disease or cardiac events.

Busulfan (Myeloablative only)

Likely Side Effects (over 10%)	Less Likely Side Effects (3-9%)	Rare Side Effects (under 2%)
• Lower white blood cell count with increased risk of infection • Diarrhea • Vomiting and nausea • Liver damage • Lower sperm production in men • Hair loss • Loss of appetite • Missing or stopping menstrual cycle in women	• Sores in mouth or on lips • Blood in urine • Fatigue • Lower platelet count (mild) with increased risk of bleeding, especially with an injury like falling • Darkening of nail beds •	• Lung fibrosis with cough and shortness of breath • Heart failure with high doses • Decrease in sodium level in the blood with high doses • Secondary cancers

Busulfan can increase your chance of having seizures. Treatment with dilantin an antiseizure medication both prior to and during busulfan treatment can decrease your chance of having seizures.

Cyclophosphamide (Cytoxan) (Myeloablative only)

Likely Side Effects (over 10%)	Less Likely Side Effects (3-9%)	Rare Side Effects (under 2%)
• Nausea and vomiting • Diarrhea • Loss of appetite • Low white blood cell count with increased risk of infection • Lower sperm production in men • Hair loss • Liver problems • Missing or stopping of menstrual periods in women	• Anemia • Low platelet count with increased risk of bleeding • Sores in mouth or on lips • Blood in urine • Fatigue • Darkening of nail beds • Fetal damage if pregnancy occurs while taking cyclophosphamide	• Lung fibrosis with cough and shortness of breath • Heart failure with high doses • Decrease in sodium level in the blood with high doses • Secondary cancers

Cyclophosphamide can cause bleeding in your bladder. Getting more fluid through a vein or your catheter and drinking extra liquids may prevent this.

Fludarabine (reduced intensity and myeloablative cord blood)

Likely Side Effects (over 10%)	Less Likely Side Effects (3-9%)	Rare Side Effects (under 2%)
• Low white blood cell count with increased risk of infection • Low platelet count with increased risk of bleeding • Anemia	• Nausea and vomiting • Diarrhea • Fatigue	• Rash • Visual changes • Numbness and tingling in hands or feet • Severe problems with brain (coma at high-dose, confusion) • Pneumonia • Irregular heart beats • Renal failure

Methotrexate (related and unrelated donors)

Likely Side Effects (over 10%)	Less Likely Side Effects (3-9%)	Rare Side Effects (under 2%)
• Nausea and/or vomiting • Loss of appetite • Mouth sores that are painful	• Low white blood cell count and increased risk of infection • Lower platelet count with increased risk of bleeding	• Damage to the liver (may be permanent or cause death) • Allergic inflammation of the lung with fever, cough, and feeling short of breath

	• Diarrhea or loose stools • Kidney damage (may be permanent) • Greater risk of sunburn • Skin changes in areas where previous radiation was given	• Hair loss • Skin reactions (rash, itching) • Feeling dizzy • Blurred vision • Hard to think • Headaches • Redness of eyes and maybe itching but not serious conjunctivitis

Tacrolimus (related and unrelated donors)

Likely Side Effects (over 10%)	Less Likely Side Effects (3-9%)	Rare Side Effects (under 2%)
• Hypertension (high blood pressure) • Tremor (shaking of the hands) • Altered levels of magnesium, calcium, potassium, and sugars in the blood	• Headache • Pain in the hands and/or feet[1] • Increases in cholesterol and triglyceride • Nausea/vomiting • Changes in how clearly one can think • Trouble sleeping • Increased hair growth • Destruction of red blood cells (hemolysis)	• Seizures • Renal failure from damage to the blood vessel walls and destruction of red blood cells by a condition called hemolytic uremic syndrome (HUS)

[1]The pain decreases or goes away with the improvement of GVHD, with a decrease in the rate of infusion, or when the tacrolimus is switched from the intravenous (by vein) to the oral form.

Mycophenolate Mofetil (MMF) (cord blood only)

Likely Side Effects (over 10%)	Less Likely Side Effects (3-9%)	Rare Side Effects (under 2%)
• Nausea • Miscarriage or birth defects if become pregnant while taking and within 6 weeks after stopping MMF	• Vomiting • Diarrhea (loose stools) and abdominal discomfort • Lower red blood cell count that is reversible • Lower white blood cell count with increased risk of infection	• Stomach and bowel bleeding (blood in stools) • Secondary cancers • Progressive multifocal leukoencephalopathy (a serious brain infection that can cause weakness, clumsiness and confusion and can lead to death)

Melphalan (reduced intensity)

Likely Side Effects (over 10%)	Less Likely Side Effects (3-9%)	Rare Side Effects (under 2%)
• Vomiting • Nausea • Mouth ulcers • Diarrhea • Skin redness • Hair loss • Loss of appetite • Fatigue • Change in taste of food • Nail discoloration	• Pulmonary scar tissues to form	• Confusion and coma • Lowers the white blood cell count, which, in turn, increases the risk of infection, which can be life threatening • Lowers the platelet count (necessary for blood clotting) which may lead to serious or life-threatening bleeding complications.

Granulocyte Colony Stimulating Factor (G-CSF) (cord blood only)

Likely Side Effects (over 10%)	Less Likely (1-10%)
• Muscle aches or pain • Bone pain • Itching • Skin rashes • Headache	• Blood vessel inflammation • Ruptured spleen

Total body irradiation (TBI) (reduced intensity cord blood only)

Likely Side Effects (over 10%)	Less Likely Side Effects (3-9%)
• Nausea • Fatigue • The irradiation dose used may result in sterility, and there is a risk of major genetic damage to any children conceived after transplantation	• Temporary hair loss • Vomiting • Cataracts (an opacity or whitening of the lens) may develop in the eye • Inflammation of the salivary gland • Diarrhea • Painful swelling of the parotid gland (a gland under the chin) for a few days • Secondary cancers • Mucositis (temporary damage to the lining of the mouth)

Total body irradiation (TBI) destroys both the abnormal and normal marrow, resulting in a loss of red blood cells, white blood cells, and platelets. The temporary absence of these blood cells produces a risk of anemia, infection, and/or bleeding. This continues until the transplant begins to work. Blood transfusions are given as needed.

You will also receive procedures such as CT scans, chest x-rays based on medical necessity and to help follow your progress. These studies are a routine part of care following transplant and expose you to more radiation, but the amount of radiation from these tests are small in comparison to the therapy dose and are not expected to increase your health risk.

You will also be receiving spleen imaging at baseline, between day 80 and 100 and at 1 year, for assessment of your spleen size and to look for myelofibrosis outside the bone marrow. This will be done either by ultrasound or CT scan or MRI scan. An MRI scan is a painless radiology technique that has the advantage of avoiding x-ray radiation exposure. There are no known side effects of an MRI scan. The benefits of an MRI scan relate to its precise accuracy in detecting structural abnormalities of the body. Patients who have any metallic materials within the body must notify their physician prior to the examination or inform the MRI staff. Metallic chips, materials, surgical clips, or foreign material (artificial joints, metallic bone plates, or prosthetic devices, etc.) can significantly distort the images obtained by the MRI scanner. Patients who have heart pacemakers, metal implants, or metal chips or clips in or around the eyeballs cannot be scanned with an MRI because of the risk that the magnet may move the metal in these areas. Similarly, patients with artificial heart valves, metallic ear implants, and bullet fragments cannot be scanned with an MRI because of the risk that the magnet may move the metal in these areas.

Late Complications from radiation:

- Sterility
- Hypothyroidism
- Possible increased incidence of radiation or chemotherapy-induced cancer, or leukemia [rare]
- Possible brain injury [rare]

You will be watched for these side effects and treated as they occur. Follow-up care in the hospital and later in the outpatient clinics will be necessary to observe your recovery and monitor for any possible late side effects of your transplant.

Risks of bone marrow, blood stem cell, and cord blood transplant in general:

GVHD: This occurs when the donor's white blood cells recognize your body as "foreign." The donor's cells then attack the cells of your body. GVHD can be mild or severe. In the most severe cases, it can cause death. You will be watched closely for this complication and given specific treatment to prevent and treat it. GVHD is treated with drugs that weaken the immune system. This makes you more likely to get infections. Treatment of GVHD may last from months to years. One of the most common treatments for GVHD is prednisone. Prolonged treatment with prednisone may result in cataracts, bone loss, diabetes, high blood pressure, bone fracture, and muscle loss.

There are two forms of GVHD: acute (early) and chronic (late) GVHD. Chronic GVHD occurs most commonly in patients who have had acute GVHD but may occur in patients who did not have any acute GVHD.

Symptoms of early or acute GVHD (seen in 70-80% of patients)

- Skin rash
- Diarrhea
- Nausea and vomiting

- Abdominal pain or cramping
- Increased risk of infection
- Liver disease (inflammation of the liver and yellowing of the skin)

Symptoms of late or chronic GVHD (seen in 50-60% of subjects)

- Skin rash
- Hair loss
- Thickened skin
- Dry mouth and dry eyes
- Increased risk of infection
- Liver disease or inflammation
- Lung disease (scarring of the lungs)
- Diarrhea

The side effects associated with transplantation can be uncomfortable, and in some cases dangerous, life-threatening, or fatal. Because this is a research study there may be additional side effects, which are not known at this time. The known or possible side effects of the treatments you will receive as part of this study are listed below. If we learn about other side effects, we will tell you.

Graft failure: This occurs when your body does not accept the transplanted cells. Graft failure may occur in 5-15% of patients. We do not know how likely graft failure is when giving ruxolitinib during and following transplant. It is also possible that the blood stem cells will grow, but not work normally. This will result in low blood counts for a long period of time. If graft failure occurs, you may be able to have a second transplant with cells from the same donor or from another donor, if another donor is available. Graft failure may result in death from infections, anemia or bleeding.

Damage to the vital organs in your body: This could affect any organ in your body such as heart, lungs, liver, gut, kidneys and bladder, brain, etc. Some subjects will experience severe lung problems due to infections and/or due to a reaction of the lungs to the chemotherapy and/or radiation. Some subjects can suffer sinusoidal obstruction syndrome of the liver (SOS). SOS is damage to the liver that can occur as a result of transplant. Symptoms and signs include yellowing of the skin (jaundice), a swollen and painful liver, fluid retention, weight gain and abnormal liver tests. In severe cases, SOS can lead to liver failure or even cause death.

Serious infections: Your immune system will be not be normal for many months after the transplant, and the white blood cells that fight infection will be very low or not function well. During this time, there is an increased risk of viral, fungal or bacterial infections. You will be prescribed certain medications to reduce the chance of those infections. However, preventive treatments are not always effective. If you develop an infection you may have to stay in the hospital longer or be re-hospitalized after transplant. Infections can be very serious or cause death.

Recurrence of cancer: There is a chance that the transplant will not cure your disease or that it returns even if the transplant is initially successful.

Genetic disease transmission: It is very rare, but there is the potential that diseases derived from the donor such as acute leukemia in adult donors and genetic diseases such as thalassemia or Gaucher's disease from cord blood donors may be passed to you through the transplanted stem cells. Each umbilical cord blood unit can only be tested for a few of the many possible genetic diseases. We will do our best to obtain screening results from the cord blood banks for diseases like thalassemia and sickle cell anemia, but they may not always be available. The family of each umbilical cord blood donor has been asked about the development of medical problems or known genetic diseases within the family to further reduce the possibility of genetic disease transmission (i.e., passage of a disease to you from the umbilical cord blood cells).

Incorrect labeling of the UCB: Though rare, it is possible that incorrect labeling of an umbilical cord blood unit could occur so that you receive the wrong unit. To avoid this, the umbilical cord blood unit is re-typed to confirm that the tissue type of the donor is as previously reported when the cord blood unit was first identified. Every cord blood unit will undergo confirmatory tissue typing either here or at an outside lab. Every effort will be made to perform the confirmatory typing in our lab, but this may not be possible if the umbilical cord unit does not have an attached sample to use. If this is the case, there are several ways the unit labeling can be confirmed.

Other Complications: Other complications that can result from the transplantation procedure not specifically related to one specific drug or the cord blood stem cells or this study include:

Rare allergic reactions: Allergic reactions to the drugs used in this study are very rare but possible.

Risk to the unborn: The treatments in this study have NOT been proven to be safe at any stage of pregnancy. Some are known to cause a miscarriage and birth defects if a woman becomes pregnant while being treated and for some time after stopping the treatment. Therefore, if you are pregnant, intend to become pregnant, or are nursing, you are not eligible for this study. Women who have the potential of becoming pregnant must use a combination of two forms of effective birth control. Effective birth control would be defined as the following: 1) refraining from all acts of vaginal intercourse (ABSTINENCE); 2) consistent use of birth control pills; 3) injectable birth control methods (Depo-Provera, Norplant); 4) tubal sterilization or male partner who has undergone a vasectomy; 5) placement of an IUD (intrauterine device); and, 6) use, with every act of intercourse, of a diaphragm with contraceptive jelly and/or condoms with contraceptive foam.

Sterility and future childbearing potential for men and women: Chemotherapy and/or radiation may affect fertility. Male patients may become sterile (unable to produce sperm). Female patients may find that their menstrual cycle becomes irregular or stops permanently. However, this DOES NOT MEAN THAT YOU CANNOT BECOME PREGNANT, and you must use some effective method of birth control. Damage to reproductive tissue may result in birth defects or permanent inability to father a child or become pregnant. You should discuss these risks and options in detail with your doctor before entering this study.

Central venous catheter: There has been considerable experience with central venous catheter use. The most common complications are clotting and local infection which often leads to a generalized infection in the blood. Clotting may require the catheter to be removed or treatment with a fibrinolytic agent (medicines that dissolve blood clots). Infections will be treated with antibiotics, and sometimes, removal of the catheter is required. Occasionally, skin redness at the catheter exit site occurs, this may require antibiotic treatment. There is also a small risk of puncturing the lung at the time of the catheter insertion. If this occurs, placement of a temporary chest tube to reinflate the lung may be required. There are no long-term effects once the lung puncture has resolved.

Non-physical risks

If you join this study, non-physical risks are:

- You might not be able to work.
- Results of genetic tests might be released by accident. This risk is very low, because we keep personal information private. If these results became known, you could have problems from others knowing about your genetic test results. For example, the results could cause stress or anxiety in family members who learn about their own risk of developing disease, or you could have problems with insurance because of your health status.

What are the benefits?

We do not know if this study would help you. We are testing ruxolitinib to see its effects on people with myelofibrosis. You might get better if you receive ruxolitinib, but your condition could stay the same or even get worse. We hope the information from this study will help other people with myelofibrosis in the future.

You have other choices besides this study.

You do not have to join this study. You are free to say “yes” or “no”. Your regular medical care would not change if you decide to say “no”.

You have other choices for treatment. Each of these choices has risks and benefits. You should talk to your doctor or healthcare provider about these choices.

Other choices include:

- Bone marrow transplant, blood stem cell transplant, or cord blood transplant that is not part of this research study;
- Another research study;
- No treatment;

- Comfort Care.

Enrollment in this study may exclude you from other research studies.

Protecting Privacy as an Individual and the Confidentiality of Personal Information

If you join this study, some people or organizations might need to look at your medical records and research records for quality assurance or data analysis. They include:

- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Center IRB. An IRB is a group that reviews the study to protect the rights and welfare of research participants.
- Fred Hutchinson Cancer Center and University of Washington.
- Office for Human Research Protections, Food and Drug Administration, and other regulatory agencies as required.
- National Marrow Donor Program (NMDP). The NMDP is a nonprofit organization that operates the Be The Match Registry® of volunteer stem cell donors and umbilical cord blood units in the United States.
- Data Safety Monitoring Board.

We will do our best to keep personal information confidential. But we cannot guarantee total confidentiality. Personal information may be given out if required by law. For example, workplace safety rules may require health workers to contact you about lab tests. Or a court may order study information to be disclosed. Such cases are rare.

We will not use personal information in any reports about this study, such as journal articles or presentations at scientific meetings.

If you join this study, information about your participation would be made part of your permanent medical record. This information would include a copy of this consent form. If an insurance company or employer or anyone else were authorized to see your medical record, they would see a copy of this consent form.

How is my genetic information protected?

A federal law called the Genetic Information Nondiscrimination Act (GINA) helps protect genetic information about people who join research studies.

GINA restricts access to genetic information so that it cannot be used for health insurance coverage decisions. GINA prevents health insurance companies or group health plans from:

- Asking for genetic information obtained in research studies, or

- Using genetic information when making decisions regarding your eligibility or premiums

GINA *does not* help or protect against genetic discrimination by companies that sell life, disability or long-term care insurance.

Would we pay you if you join this study?

There is no payment for being in this study.

Would you have extra costs if you join this study?

- If you join this study, you may have a co-payment for ruxolitinib. Your clinical team will work with your insurance company to decrease any extra costs if possible.

You will **not** be billed for research blood and marrow samples. These are paid for by the study.

If you have questions regarding your costs, financial responsibilities, and/or medical insurance coverage for this activity, please ask your physician or inquire at the FHCC Patient Financial Services Department at 206-606-1113.

What if you get sick or hurt after you join this study?

For a life-threatening problem, call 911 right away or seek help immediately. Contact your study doctor when the medical emergency is over or as soon as you can.

For all other medical problems or illness related to this research, immediately contact Dr. Rachel Salit. They will treat you or refer you for treatment. You or your health insurance will have to pay for the treatment. There are no funds to pay you for a research-related injury, added medical costs, loss of a job, or other costs to you or your family. State or national law may give you rights to seek payment for some of these expenses. You do not waive any right to seek payment by signing this consent form.

You or your insurer will be billed for treatment of problems or complications that result from your condition or from standard clinical care.

You would not lose any legal right to seek payment for treatment if you sign this form.

What will my information and/or tissue samples be used for?

Your information and samples (such as blood and bone marrow) will be used for the purposes of this study.

Your samples might help researchers develop new products. This research could be done by for-profit companies. There is no plan to share with you any revenue generated from products developed using your tissue samples.

During this study, if the researchers learn new information that may be important to your general health or to your disease or condition, they will share that information with you.

We invite you to donate leftover samples for other research.

After we do tests on samples in this study, some samples may be left over. We invite you to donate this leftover sample for future research. This may include genetic research.

If you join this study, you would not have to donate samples for future research. You would be free to say "yes" or "no." Regular medical care would not change if you say "no."

If you donate samples, it would be stored in a secure location. If we want to use your samples for other research or share it with other scientists for research, an ethics review committee (IRB) would review the request. The IRB would decide if we need to ask you for permission to do the research.

Your donated samples would be used only for research. This research could be done by for-profit companies. Researchers would not report their results to you or your doctors. The research results would not be included in medical records. The results would not affect your medical care.

Research with samples might help develop new products. If these products make money, there is no plan to share the money with the participants who donate the samples.

If you donate samples for research, you could withdraw the donation at any time by calling Dr. Rachel Salit at 206-667-1317 or email at rsalit@fredhutch.org. You would have no penalty for withdrawing the donation, and regular medical care would not change. We could not return donated samples, but we might be able to destroy the donated samples. We could not destroy samples if they are stored or shared without any label saying who donated it. In this case, it could still be used for research.

Your rights

- You do not have to join this study. You are free to say "yes" or "no".
- If you get sick or hurt in this study, you do not lose any of your legal rights to seek payment by signing this form.
- During the study, we might learn new information that you need to know. For example, some information may affect your health or well-being. Other

information might make you change your mind about being in this study. If we learn these kinds of information, we would tell you.

- If you join this study, you would not have to stay in it. You could stop at any time (even before you start). Your regular medical care would not change. You would have no penalty for stopping, but it would be better not to join the study if you think that you would change your mind later.

- If you decide to drop out, we would want you to tell the study doctor. The doctor could tell you about the effects of stopping ruxolitinib (without tapering). You and the doctor could talk about the follow-up care and testing that would help the most.

- Before you leave the study, the doctor might ask you to sign a separate consent form to continue in the follow-up part of the study.

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.

Your responsibilities

If you join this study, you would have some responsibilities.

- Follow the schedule of study visits and procedures.
- Take study medications as directed.
- Prevent pregnancy.
- Tell us about side effects.

For more information

If you have questions or concerns about this study, you can talk to your doctor anytime. Other people you could talk to are listed below.

If you have questions about:	**Call:**
This study (including complaints and requests for information)	206-667-1317 (Dr. Rachel Salit, MD)
If you get sick or hurt in this study	206-667-1317 (Dr. Rachel Salit, MD)
Your rights as a research participant	206-667-5900 or email irodirector@fredhutch.org (Director of Institutional Review Office, Fred Hutchinson Cancer Center)
Your bills and health insurance coverage	206-606-1113

Emergency number (24 hours): 206-598-8902

Do you agree to donate your leftover samples (either fluid or tissue samples) for future research? (Circle one)

YES **NO**

Signatures

Please sign below if you:

- have read this form (or had it read to you);
- had the opportunity to ask any questions you have;
- had the opportunity to discuss the research with the person obtaining consent; and
- agree to participate in this study.

Participant (age 18+):

Printed Name	Signature	Date

Legally Authorized Representative: Please sign below if you:

- have read this form (or had it read to you);
- had the opportunity to ask questions;
- had the opportunity to discuss the research with the person obtaining consent; and
- agree to consent on behalf of the participant for him or her to participate in this study.

Legally authorized representative:

Printed Name	Signature	Date

Relation to the participant

If you served as an interpreter or impartial witness during the consent process, sign below to indicate you attest to the accuracy of the presentation and the participant's apparent understanding of and willingness to participate in the research.

Impartial Witness or Interpreter:

Printed Name	Signature	Date

Researcher's statement

I have discussed the research study, including procedures and risks, with the person signing above. A copy of the signed consent form will be given to the participant.

Person obtaining consent signature:

Printed Name	Signature	Date

Protocol: 10093
Current consent version date1/17/2025
Previous consent version date: 2/23/2024
Copies to: Participant, medical record