FRED HUTCHINSON CANCER CENTER
UNIVERSITY OF WASHINGTON SCHOOL OF MEDICINE,
Protocol 9816

Consent to Participate in a Research Study called: A Randomized Phase II Study to Compare the Net Clinical Benefit of Cyclosporine and Sirolimus combined with MMF or Post-Transplant Cyclophosphamide as GVHD prophylaxis after HLA-Matched Unrelated or HLA-Mismatched G-CSF Mobilized Blood Cell Transplantation using Nonmyeloablative or Reduced Intensity Conditioning for Patients with Hematologic Malignancies

Note: If you are serving as a legally authorized representative and have been asked to sign this form, the 'you' in this document refers to the patient.

- **Who is in charge of this research study?**

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➢ Why have I been asked to take part in this research study, and who is conducting it?

You are being asked to take part in this study because you have a severe blood cancer that may be treatable with a blood stem cell transplant from an unrelated donor. Because of your age or underlying health, you may have a higher likelihood of experiencing harm from a conventional stem cell transplant, so a nonmyeloablative or reduced-intensity blood stem cell transplant is being offered to you. Nonmyeloablative and reduced-intensity stem cell transplants use lower doses of chemotherapy or radiation than conventional (standard) stem cell transplants. This research study looks at ways to prevent a common but very serious complication following transplantation. This complication is called "graft versus host disease" or "GVHD" and is described in detail below. We do not guarantee or promise that the treatment or procedures described in this study will be effective in treating your medical condition. This study is being performed here at the Fred Hutchinson Cancer Center. . The Investigators of this study want you to understand that patients in clinical trials include only those who are completely informed and choose to participate. Please take your time to make your decision about whether to participate. We encourage you to discuss your decision with your doctor, family and friends.

➢ Why is this research study being done?

Graft versus host disease (GVHD) is one of the main complications following transplantation. GVHD can occur early after the transplant (called acute GVHD) or late after transplant (called chronic GVHD). This is a process where donor cells may react against cells of your body causing inflammation that can involve the skin, liver and gastrointestinal system. GVHD is associated with a greater risk of dying from complications after the transplant.

Various medications that suppress the immune system are used to try to prevent GVHD from developing. The best combination of immune suppressing drugs is not known; therefore the purpose of this clinical trial is to evaluate two different combinations of commonly used immune suppressing drugs to try to determine if one combination is better than another at preventing GVHD.

Two drugs, cyclosporine (CSP) and sirolimus (SIR), will be combined with **either** mycophenolate mofetil (MMF) or post-transplant cyclophosphamide (PTCy) in two different treatment regimens, henceforth referred to as treatment arms: Arm 1 will use CSP, SIR, and MMF. Arm 2 will use CSP, SIR and PTCy. PTCy is associated with less chronic GVHD in recent studies, but it could potentially cause more chemotherapy-related toxicity compared to MMF. It is also unknown how Arm 1 or 2 may differ in other outcomes of transplant such as relapse and graft function. In this trial a computer will randomly choose which combination of immunosuppressive drugs you will receive. A detailed plan of the two different treatment schedules is shown in the table below.

Conditioning and Immunosuppression Schedule

	Immune suppressive drug	Start of immune suppressive drug	After transplantation we will start reducing your dose on day	The immune suppressing drug is stopped at post-transplantation day
Treatment Arm 1 (HLA-Matched Unrelated Donor)	CSP	Day 3 before transplantation	96	150
	SIR	Day 3 before transplantation	150	180
	MMF	Day of transplantation	30	40
Treatment Arm 2 (HLA-Matched Unrelated Donor)	CSP	Day 5 after transplantation	96	150
	SIR	Day 5 after transplantation	150	180
	PTCy*	Day 3 and 4 after transplantation	Not applicable	Not applicable
Treatment Arm 1 (HLA-Mismatched Unrelated Donor)	CSP	Day 3 before transplantation	150	180
	SIR	Day 3 before transplantation	180	365
	MMF	Day of transplantation	30	150
Treatment Arm 2 (HLA-Mismatched Unrelated Donor)	CSP	Day 5 after transplantation	150	180
	SIR	Day 5 after transplantation	180	365
	PTCy*	Day 3 and 4 after transplantation	Not applicable	Not applicable

* For patients receiving PTCy, the start day of the PTCy and CSP/SIR may vary by one day depending on when the stem cells are infused.

➢ How many people will take part in the study?

Up to 160 patients will take part in the study.

➢ What tests, procedures, and treatments are part of this study?

Standard procedures that will be done as part of pretransplant evaluation:
First we will need to find out whether you can be enrolled in this study. You will be asked to give information about your medical history and undergo the exams and tests listed below. If you have had any of them recently, your doctor may decide not to repeat them. The exams and tests may include the following, depending on your underlying cancer:

- Bone marrow biopsy
- Creatinine clearance
  (Evaluates kidney function)
- Blood tests
- Chest x-rays and pulmonary function tests or 6-minute walk tests.
  (Evaluates lung function)
- Electrocardiogram and MUGA scan or echocardiogram
  (Evaluates heart function)
- CT-scan
  (Method used to obtain X-ray images lymph nodes and organs)

These exams and tests are not experimental; they are routine. They are standard good medical care even if you do not join the study. If you do join, some of these procedures may be done more often

than if you were not taking part in the study. The tests may be done on an outpatient basis at your doctor's office or clinic, or in a hospital.

Standard procedures that will be done as part of the transplantation:

Stem cell transplantation: Peripheral blood stem cells will be used in this study. Peripheral blood stem cells are collected from the blood of the donor after treatment with a drug called a growth factor. Like a blood transfusion these cells are infused into you, where they will begin to produce new blood cells.

Conditioning is the chemotherapy with or without radiation necessary to enable the blood stem cell transplant to work. You will receive one of 2 different conditioning types based on what your treating physician decides is best for your disease and overall condition. These are: A) Fludarabine, melphalan and low-dose total body irradiation (TBI), and B) Fludarabine and low-dose TBI. The type of conditioning regimen planned will not influence which immunosuppression regimen you receive on this study.

To reduce the risk of GVHD you will receive immune suppressive drugs in accordance to the treatment arm you have been assigned. This part of the transplantation procedure is the main research focus of the study and is explained in the section above (section: Why is this research study being done)

Donor lymphocyte infusion: Donor lymphocytes are a collection of white blood cells that are collected from the donor. Donor lymphocyte infusions (DLI) may be effective in some patients with relapsed cancer after a bone marrow transplant. DLI can also be given when there appears to be a risk of rejection of the donor graft. The current procedure is that a portion of the peripheral blood stem cells will be separated, cryopreserved, and stored in case DLI is required. If DLI is necessary to treat your underlying malignancy or prevent rejection, you will be offered DLI on another protocol or treatment plan.

Blood and Bone Marrow Tests

You will have blood tests at least three times a week to check kidney function and blood cell counts early after the transplant. Other blood tests will be done periodically to check your liver function and electrolytes. A bone marrow aspirate may also be required at various time points to check for the presence of donor cells and cancer.

These exams and tests are not experimental; they are routine. They are standard good medical care even if you do not join the study and may be done on an outpatient basis at your doctor's office or clinic, or in a hospital. However, some of these procedures may be done more often than if you were not taking part in the study.

Molecular Test of Disease Response: Certain blood cancers can be monitored by special tests. One of these tests detects DNA of the tumor cells. This test is highly sensitive and may be used for monitoring the response of your cancer to the stem cell transplant. This test will be performed using peripheral blood and bone marrow samples. This test will not add to the frequency of standard blood or bone marrow tests scheduled to monitor the response of the leukemia to the stem cell transplant. Some of these tests are still experimental and, therefore, the results of the unapproved tests will not be used for clinical decision-making and will not be routinely made available to you.

Molecular Test of Donor Engraftment: The percentage of donor cells in your blood and marrow, can be monitored by special tests that detect the DNA of the donor cells. These tests, referred to as chimerism tests, evaluate the degree of donor engraftment after the blood stem cell transplant. This test will be performed using peripheral blood and bone marrow samples. This test will not add to the frequency of standard blood or bone marrow tests.

➢ **How long will I be in the study?**

Your treatment at the Fred Hutchinson Cancer Center will last approximately 3 and 1/2 months, but could be longer. You may be asked to return for follow up at 6 months and every year thereafter in order to help manage some of the complications of the transplant.

We would like to keep track of your medical condition for the rest of your life to fully understand the long-term effects of this study. However, you may be taken off the protocol and followed less frequently if one of the following happens:

- The study treatment does not work for your cancer;
- You develop a serious side effect that you cannot tolerate or that cannot be controlled with other medications;
- Your health gets worse;
- You are unable to meet the requirements of the study (for example, you cannot take the medicine as prescribed or you refuse follow-up);
- You start other treatments for your cancer;
- Other treatments for your cancer become available;
- By your request.

Your decision to participate in this study is completely voluntary. You may decide not to participate in this study at any time, for any reason, without notice. However, withdrawal from treatment during the conditioning regimen or after the stem cell transplantation could be fatal. The early discontinuation of the immune suppressing drugs cyclosporine, MMF and/or sirolimus after blood stem cell transplant could lead to rejection of the donor blood stem cells or life threatening GVHD. Prior to discontinuing the study, we request that you discuss your decision with your primary doctor and, if you wish, the research physician for this study.

What are the risks of the study?

There are risks involved in taking part in this study, and there may be side effects. Most of these risks and side effects are inherently connected to the transplantation procedure and will vary from person to person. However, as this study is evaluating new combinations of immunosuppressive drugs, it is possible side effects may be worse than listed below for the individual drugs or even unusual side effects that have not been observed before may occur. These drugs have been tested independently and in some studies in combination with each other in blood stem cell transplant patients. However, there is limited experience testing these drugs after a nonmyeloablative or reduced intensity transplant or in patients who have dysfunction of their liver or kidneys.

Your doctor may be able to change or give you medications to make some of the side effects less bothersome. If the side effects are caused by medications they often can go away shortly after the drugs are stopped. In some cases, side effects from this study such as GVHD and infections can be very serious, long lasting, and/or life threatening possibly resulting in death. Please talk with your doctor about these side effects. If you want to read more about the side effects from study drugs, please ask your doctor or pharmacist for more information.

Side effects that we know about now are described in the table. Side effects are categorized into either:

- **Likely side effects:** Side effects that may occur in 10% or more of patients (this means that 10 or more patients out of 100 might get this). Certain side-effects in this category could occur in virtually all patients.
- **Less likely side effects:** Side effects that may occur in 3-9% of patients (this means that 3 to 9 patients out of 100 might get this).
- **Rare side effects:** Side effects that do not occur very often, but may occur in less than 3% of patients (this means that 1 or 2 patients out of 100 might get this).

With any drug or combination of drugs, there may be complications or side effects that we do not know about.

Likely Side Effects	*Less Likely Side Effects*	*Rare Side Effects*
Graft-versus-host disease	Allergic reaction (including itching, hives, flushing, hypersensitivity, shortness of breath, wheezing, chest tightness, skin rashes, fever, chills, muscle stiffening, severe breathing problems)	Sores in mouth and/or throat
Nausea	Jaundice (yellowish discoloration of sclera)	Hair loss
Vomiting	Rejection/graft failure(when the body rejects the transplanted donor cells)	Skin or nail discoloration
Diarrhea	Fluid retention (bloating or swelling)	Nail changes
Loss of appetite	Weakness	Painful burning on the skin of the hands and feet
Fever	Fatigue	Irregular menses or stopping of menses
Lowered white blood cell counts (may lead to infection)	Seizure	Infertility (inability to have children) in women or Sterility for men
Lowered platelet counts (may lead to bleeding)	Tremor	Failure of heart function
Lowered red blood cell counts (may lead to anemia, fatigue, shortness of breath)	Muscle or joint pain	Bleeding or dysfunction of the central nervous system
Infection	Red blood cell destruction	Failure of brain function
Time away from work		Impairment or failure of kidney function
		Failure of lung function
		Failure of liver function

In addition to the above risks, there is the risk of organ failure, including heart, kidney, lung, brain, liver or other body parts. This risk is increased in those patients who have already had significant chemotherapy and/or radiation therapy or pre-existing damage to any organ system.

Although the aim of this study is to reduce the risks of stem cell transplants, **the side effects of treatment could be severe and include a risk of death**. In addition, the cancer may recur even if the transplant is initially successful. Furthermore, there is a possibility that this approach may be less successful at treating your cancer and the rate of cancer recurrence will be higher than a standard stem cell transplant.

Total Body Irradiation (TBI):

Likely Side Effects	Less Likely Side Effects
• Nausea (feeling sick to stomach) • Fatigue (feeling tired) • Sterility, and major genetic damage to any children conceived after transplantation	• Temporary hair loss • Vomiting (throwing up) • Diarrhea (loose stools) • Painful swelling of the parotid gland (a gland under the chin) for a few days • Cataracts (an opacity or whitening of the lens) may develop in the eye • Secondary cancers • Lung Damage

TBI may destroy normal bone marrow cells in addition to the malignant cells.

TBI has been associated with causing sterility; however, it is expected that the risk of infertility will be lower than the risk after transplants that use higher doses of TBI. Although TBI can theoretically cause abnormalities in children born to transplant survivors, the incidence of genetic abnormalities has not been reported to be greater than the general population. However, this is a potential risk and birth control should be used for at least one year after transplant to minimize risks of conceiving.

The dose of TBI used in the nonmyeloablative transplant in this protocol is approximately one-sixth of that used in conventional transplant protocols, and severe acute side effects are not expected.

You will also be receiving diagnostic exams (CT scans, chest x-rays, bone scan, etc) to help follow your progress. These exams will result in a radiation dose to you, but these doses are small in comparison to the therapy dose you will receive. They are not expected to increase your health risk.

The chemotherapy used in the conditioning regimen can cause side effects, including those listed below:

Fludarabine

Likely Side Effects (over 10%)	Less Likely Side Effects (3-9%)	Rare Side Effects (under 2 %)
• Low white blood cell count with an increased risk of infection (from bacteria, fungi or viruses) • Lower platelet count with and increased risk of bleeding • Anemia • Infections	• Nausea (feeling sick to your stomach) • Diarrhea (loose stools) • Fatigue	• Vomiting (throwing-up) • Trouble seeing or problems with your eyes • Numbness or tingling in your fingers or toes • Confusion or coma • Pneumonia

Melphalan

Likely Side Effects (over 10%)	Less Likely Side Effects (3-9%)	Rare Side Effects (under 2 %)
• Lowers white blood cell count and increased risk of infection • Bleeding from low platelet count • Constipation • Diarrhea • Hair loss • Mouth ulcers • Nausea and vomiting • Change in taste • Nail discoloration	• Abnormal heart rhythm • Liver inflammation • Kidney failure	• Allergic reaction • Interstitial pneumonia • Confusion and coma • Seizure • Lung fibrosis

***Stem Cell Transplant*:** We expect that the infusion of donor stem cells to be associated with relatively minor side effects like a blood transfusion. However, after the stem cell transplant you will be at very high risk for complications including death. Supportive care with red blood cell and platelet transfusions and antibiotic therapy may be necessary. Long-term organ damage may also occur as a result of radiation or the treatment with immune suppressing drugs. It is possible you could at some point experience side effects similar to those that occur after a stem cell transplant that uses high doses of chemotherapy including:

Likely Side Effects	Less Likely Side Effects
• Low blood counts • Fever • Chills • Nausea • Infections	• Bleeding • Failure of the donor stem cells to grow • Shortness of breath

For patients receiving unrelated transplants there is an extremely low risk that for reasons beyond our control either (i) your unrelated donor will be unable to donate stem cells or (ii) the donation will result in a product that cannot be infused safely. If either of these extremely unlikely events were to occur after you receive the conditioning regimen, there is a chance that your own marrow cells will not recover. If your own marrow cells do not recover, the only way to prevent your death would be to find a replacement donor. Finding a replacement donor soon enough to prevent death would be very difficult. Even if another donor is found, the transplant using the replacement donor's stem cells might not be successful.

***Central Venous Catheter*:** A central venous catheter is a hollow tube that is placed in a large vein inside the body. It is used to give intravenous medicine and to withdraw blood for lab tests. It is placed surgically, often using a local anesthetic (numbing medicine injected into the skin), and can cause some discomfort.

Less Likely Side Effects	Rare Side Effects
• Clotting of blood (treated with a medicine that dissolves clots) • Bleeding around the catheter • Infection in the tissues around the catheter or in the bloodstream • Skin redness at the catheter exit site, which may require treatment with an antibiotic.	• A small chance of a puncture to the lung during placement of the catheter • A blood clot can form on the tip of the catheter, break off, and go into the lungs (pulmonary embolus), which could cause shortness of breath and pain and potentially death.

Graft-versus-host disease: Graft-versus-host disease is a known complication of stem cell transplantation. Graft-versus-host disease has occurred in 50 - 70% of patients on similar protocols. GVHD may be mild or severe and may require prolonged treatment with immune suppressing drugs to reduce inflammation. Severe GVHD and complications of its treatment can result in your death.

Early or Acute GVHD:	
• Skin rash • Lack of appetite, stomach cramps, diarrhea (loose stools) or "full" feeling in stomach • Problems of the liver (such as jaundice)	• Problems of the stomach, including intestinal bleeding • Nausea (feeling sick to stomach) • Vomiting (throwing up)

Chronic GVHD may occur after transplantation and may involve any of the above, plus:	
• Problems of the eyes	• Problems of the mouth, lips, and throat
• Problems of the skin	• Dry Mouth and/or Eyes
• Problems of the liver	• Lung Damage
• Problems of the joints	• Hair Loss

Cyclosporine (CSP), mycophenolate mofetil (MMF), sirolimus (SIR), and post-transplant cyclophosphamide (PTCy) are used in different combinations in this study to prevent GVHD. The side effects of these drugs are listed below.

Mycophenolate Mofetil (MMF): MMF is a drug used for suppressing the immune system for stem cell transplantation. The drug is reasonably well tolerated by patients who have had nonmyeloablative transplants. There are a small number of patients who have received solid organ transplants and had reversible fall in their red cell or white cell count while receiving MMF. Additionally, cases of Pure Red Cell Aplasia (PRCA) have been reported in some patients receiving MMF. PRCA is a condition in which the bone marrow stops producing red blood cells. In some instances, PRCA can be reversed by reducing or stopping MMF. Your blood counts will be monitored closely and if significant decrease is noted, dose adjustments or stopping your MMF may be indicated.

Cases of progressive multifocal leukoencephalopathy (PML) have occurred in some patients receiving MMF. PML is a rare disorder that affects the central nervous system, and is most often found in patients with suppressed immune systems. It occurs when the polyomavirus (or JC virus) is activated, and can cause neurologic symptoms including weakness on one side of the body, lack of emotion, confusion, cognitive difficulties, and loss of coordination. It can cause permanent disability and is sometimes fatal. You should notify your doctor immediately if you develop any of the above symptoms.

MMF has caused birth defects in humans. The United States Food and Drug Administration (FDA) requires that women who take part in this study must use two forms of contraception if they are fertile and not abstinent.

FOR WOMEN WHO COULD BECOME PREGNANT: Birth defects could occur if you take MMF while you are pregnant. As discussed above, you must use 2 effective forms of contraception if you are fertile and sexually active. You should talk to your doctor to find out which methods of birth control would be most effective for you. You must notify your doctor for the study immediately if you become pregnant while you are taking MMF. You should not breast feed while you are taking MMF.

Likely Side Effects	Less Likely Side Effects	Rare Side Effects
• Nausea (feeling sick to stomach)	• Vomiting (throwing up) • 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

Cyclosporine (CSP): Cyclosporine is a drug used for suppressing the immune system.

Likely Side Effects	Less Likely Side Effects	Rare Side Effects
• Nausea (oral administration) • Vomiting (oral administration) • High blood pressure (hypertension) • Shaking of hands (tremor) • Increased hair growth • Effect on mental function • Loss of magnesium, calcium, potassium	• Headache • Painful sensation in hands or feet which went away with the improvement of the GVHD or when the cyclosporine was switched from the intravenous to the oral form. • Change in liver or kidney function • Changes in how clearly one can think • Increases in cholesterol and triglyceride	• Patients have had seizures, but it is unclear whether cyclosporine, other drugs, or a combination of drugs were responsible. • Kidney damage severe enough to require the use of IV fluids or an artificial kidney machine (dialysis) • Destruction of red blood cells (hemolysis) may result in withholding cyclosporine or discontinuing it's use • Bleeding of the brain (relation to cyclosporine unknown)

If your kidney function is poor prior to transplant, there is an increased risk that you may develop kidney failure requiring hemodialysis (artificial kidney). There is a risk that a small percentage of patients may develop a secondary cancer resulting from this treatment.

Side effects of cyclosporine are generally reversible after decreasing the dose of the drug. During treatment, cyclosporine blood levels will be checked to determine if there is an increased risk of side effects that may require that the dose be changed. There is a risk that a small percentage of patients may develop a secondary cancer resulting from this treatment.

Sirolimus (rapamycin):

Likely Side Effects	Less Likely Side Effects
• Increase in blood pressure • Headache, or tremors • Altered levels of magnesium and potassium in the blood. • Decreased kidney function • If blood lipids (triglycerides and cholesterol) are increased the use of drugs to correct this problem may be necessary • Destruction of red blood cells (hemolysis) can occur with sirolimus	• Seizures • Breakdown of muscle (rhabdomyolysis) • Some patients have had seizures, but it is unclear whether sirolimus, other drugs, or a combination of drugs were responsible • Loss of kidney function • Low white blood cell count with an increased risk of infection (from bacteria, fungi or viruses) • Lower platelet count with and increased risk of bleeding • Anemia • Infections • Blurry vision

Post-transplant Cyclophosphamide (PTCy):

Likely Side Effects	Less Likely Side Effects
• Temporary hair loss • Nausea • Vomiting • Diarrhea • Loss of appetite • Sores in mouth or lips • Decreased white blood cell count with increased risk of infection • Low platelet count with increased risk of bleeding • Blood in urine	• Anemia • Damage to the fetus if you become pregnant • Temporary tiredness • Scarring of lung tissue • Secondary cancers

Some of these effects are generally reversible upon decreasing the dose or stopping the drug.

Combinations of immunosuppressive drugs: These drugs have been tested independently and in some studies in combination with each other in blood stem cell transplant patients. However, there is limited experience testing these drugs after a nonmyeloablative or reduced-intensity transplant or in patients who have dysfunction of their liver or kidneys. The goal of this study is to reduce the incidence of GVHD by giving new combination of immunosuppressive drugs and it is likely that these will be more immunosuppressive than when these drugs are given alone. Furthermore, it is possible that the combination of the immunosuppressive drugs may result in worse side effects than is listed above for the individual drugs or even unusual side effects that have not been observed. The most likely side effects from the combination of the immunosuppressive drugs are renal failure,

destruction of red blood cells, or serious infections. These side effects are often times reversible, but sometimes they are not reversible and these side effects could result in death.

Rejection of the Graft: Some patients on similar protocols who received a blood stem cell transplant from an unrelated donor had graft rejection. After rejecting the graft, most of the patients had their original blood cells grow back and recover to previous levels. Most patients required red blood cell or platelet transfusions until the blood counts recovered. About 15% of the patients that had graft rejection did not have recovery of their blood counts and died from complications of low blood counts. Therefore, there is a chance that if you have graft rejection your blood counts may not recover and you could die from this problem.

Risk to the Unborn: You should ***not*** become pregnant or father a child while on this study. The treatments in this study have NOT been proven to be safe at any stage of pregnancy. Therefore, if you are pregnant or nursing, you are not eligible for this study. Women who have the potential of becoming pregnant or men who have the potential of fathering a child must use two forms of effective birth control for one year after transplant. 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); 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 irradiation 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 OR FATHER A CHILD, and you must use some effective method of birth control for at least one year after the transplant. Damage to reproductive tissue may result in birth defects or permanent inability to have a child or become pregnant. You should discuss these risks and options in detail with your doctor before entering this study.

➢ **Are there benefits to taking part in this study?**

We do not know if this study would help you. We are testing two combinations of commonly used immune suppressing drugs to see its effects on people with your type of blood cancer. You might get better with the immune suppressing drug regimen you receive, but your condition could stay the same or even get worse. We hope the information from this study will help other people with blood cancers in the future.

➢ **What if new information is learned while I am in this study that might affect my health?**

If we learn any important new information that might affect your health, welfare, safety, or willingness to stay in the research study, your doctor (physician) will tell you. You may be asked to sign another consent form if you wish to stay in the research study at that time.

➢ **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.

Instead of being in this study, you can decide to have:

- Chemotherapy with other drugs known to be effective for your underlying cancer.
- A stem cell transplant on another protocol or treatment plan.
- No treatment.

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:

- Researchers involved with this study
- The Fred Hutchinson Cancer Center (FHCC)
- University of Washington (UW)
- The National Cancer Institute (NCI)
- The Food and Drug Administration (FDA)
- National Institutes of Health (NIH)
- U.S. Office for Human Research Protections (OHRP)
- Institutional Review Board (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.
- Data and Safety Monitoring Board (DSMB)
- National Marrow Donor Program

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 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.

We have a Certificate of Confidentiality from the National Institutes of Health (NIH). This Certificate helps us protect the privacy of people who join this study. If you join the study, the Certificate means that generally we would not have to give out identifying information about you even if we were asked to by a court of law. We would use the Certificate to resist any demands for identifying information.

We could not use the Certificate to withhold research information if you give written consent to give it to an insurer, employer, or other person.

This protection has some limits. We would voluntarily provide the information:

- To a member of the federal government who needs it in order to audit or evaluate the research.
- To individuals at the University of Washington, the funding agency, and other groups involved in the research, if they need the information to make sure the research is being done correctly.
- To the federal Food and Drug Administration (FDA), if required by the FDA.
- To someone who is accused of a crime, if he or she believes that our research records could be used for defense.
- To authorities, if we learn of child abuse, elder abuse, or if patients might harm themselves or others.

➢ **Would we pay you if you join this study?**

You will not be paid for taking part in this study.

➢ **What are the costs?**

You or your insurance company will pay for all medical expenses relating to, or arising from, this study. You and your insurance company will not be charged for those tests that are considered experimental. If you are injured or become ill from taking part in this study, emergency medical treatment is available but will be provided at the usual charge. No funds have been set aside to pay you in the event of injury. You or your insurance company will be charged for continuing medical care and/or hospitalization. Taking part in this study *may* lead to added costs for you or for your insurance company due to the frequency of blood tests required. If you have any questions concerning your costs, financial responsibilities, and or medical insurance coverage for this activity, please ask your physician or contact the FHCC Patient Financial Services Department at (206) 606-6226.

➢ **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 the emergency number at 206-598-8902. 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.

➢ Do I have to be part of the study?

You do not have to participate in this study. Your decision to participate is completely voluntary and should only be made when you have a complete understanding of all treatment options and of the risks involved in participating in this study.

If you have questions about the study, please talk with your physician or one of the investigators listed at the beginning of the consent. Do not sign this form unless you have had the chance to ask questions and have received satisfactory answers. You may also wish to discuss this matter with a relative, or friend.

➢ What are my rights as a study participant?

- 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.

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.
- Takes study medications as directed.
- Prevent pregnancy.
- Tell us about side effects.

➢ **Who can I call if I have questions or problems?**

For Questions About	Please Contact
This study and what it involves	Your doctor (physician) or one of the investigators listed at the beginning of the consent
Your rights as a participant in a research study	206-667-5900 or email irodirector@fredhutch.org (Director of Institutional Review Office, Fred Hutchinson Cancer Center)
Your bills and health insurance coverage	Patient Financial Services at 206-606-6226
Research related injury	Your physician or one of the investigators listed at the beginning of this consent
Emergency care	**Emergency (24 hour) phone**: UWMC (206) 598-8902;
Medical records	Contact the Director of Health Information Management at 206-606-2174.

➢ **Where can I get more information about cancer and its treatment?**

You can call the Cancer Information Service at 1-800-4-CANCER or visit the National Cancer Institute's Clinical Trials Web Site at http://cancertrials.nci.nih.gov.

You can also visit the NCI's Web sites…cancernet™: comprehensive clinical trials information http://cancernet.nci.nih.gov.

If you would like additional information about the drugs used in this trial and their side effects, you should ask your doctor or pharmacist. You can also get information at any time from the doctor in charge of your medical care in this study or one of the study investigators.

You will get a copy of this form. You may also request a copy of the protocol.

CONSENT TO PARTICIPATE IN THE RESEARCH STUDY

I have carefully read this consent form. This study has been explained to me. I understand that it is my choice whether or not to take part in this study. I am aware of the possible risks and benefits of taking part in this study. I have had the chance to ask questions about it, and all questions were answered to my satisfaction. I now agree to take part in this research study.

I also give permission to the people and organizations connected with this research study to review and copy my research records, both during the research and the long-term follow-up.

_____

Research Participant / Printed Name, Signature, and Date

_____

Legally Authorized Representative*
Printed Name, Signature, and Date

*** If you are not the person taking part in this study, please state your relationship to that person (e.g., legally authorized representative):**

_____

If you served as an interpreter or witness during the consent process, sign below to indicate you attest to the accuracy of the presentation to the participant and the apparent understanding of the research by the participant.

_____

Witness or Interpreter / Printed Name, Signature, and Date

MEDICAL STAFF PERSON'S STATEMENT

I have discussed the above research study, including the study purpose, procedures, risks and benefits, and possible alternatives, with the person signing above. All the elements of informed consent were reviewed and discussed with the subject. Special concerns that the participant expressed were noted and appropriately addressed. I encouraged questions and have answered all questions to the best of my ability. The participant is aware that he/she has a choice in taking part in this study. A signed copy of the consent form will be given to the participant.

_____

Medical Staff Person's Signature / Printed Name, Signature, and Date

_____

Signature of Any Additional Staff Person Present During Consent Process (if present)

Current Version: 08/21/2023
Previous Version: 05/17/2023
Copies to: Patient, Medical Records, Research File

Signed Consent <u>MUST</u> be sent to Data Management – Mail Stop LF-229
FHCC, 1100 Fairview Ave N, Seattle, WA 98109-1024