FRED HUTCHINSON CANCER RESEARCH CENTER
UNIVERSITY OF WASHINGTON SCHOOL OF MEDICINE,
DEPARTMENT OF MEDICINE, DIVISION OF ONCOLOGY
SEATTLE CHILDREN'S

Consent to Participate in a Research Study called: A Phase I/II Study Evaluating the Safety and Efficacy of Adding a Single Prophylactic Donor Lymphocyte Infusion (DLI) of Natural Killer Cells Early After Nonmyeloablative, HLA-Haploidentical Hematopoietic Cell Transplantation – A Multi Center Trial

Note: If you are a parent or guardian of a patient younger than 18 years old and have been asked to sign this form, the 'you' in this document refers to the patient.

Investigators (doctors in charge of this study):

Brenda Sandmaier, M.D.,	Member, FHCRC, Professor of Medicine, UW
Shelly Heimfeld, PhD	Member, FHCRC
Effie Petersdorf, MD	Member, FHCRC, Professor of Medicine, UW
Ann Woolfrey, M.D.	Member, FHCRC, Professor of Pediatrics, UW
Michael Linenberger M.D.	Associate Member, FHCRC, Professor of Medicine, UW
Mohamed Sorror, M.D., MSc	Associate Member, FHCRC, Associate Professor of Medicine, UW
David Maloney, MD, PhD	Member, FHCRC, Professor of Medicine, UW
Rainer Storb, M.D.	Member/Program Head, Transplantation Biology, FHCRC, Professor of Medicine, UW

Statistician: Barry Storer, PhD, Member, FHCRC

Additional Performance Sites	Investigators	Emergency Phone Numbers
Medical College Wisconsin - Children's Hospital of Wisconsin	Monica Thakar, MD	(414) 456-7546
Medical College of Wisconsin–Froedert Hospital	Parameswaran Hari, MD	(414) 805-4600

Research Nurse: Michelle Bouvier, RN (206) 667-6993, pager (206) 995-7658

Emergency 24 Hour Phone:

FHCRC:	Phone:	(206) 598-8902	FAX: (206) 598-4034
Seattle Children's:	Phone:	(206) 987-2000*	FAX: (206) 987-2764

*Ask Seattle Children's Operator for "Transplant Provider On-Call"

The purpose of this informed consent form is to let you know about a clinical trial (a type of research study). This form tells you about the purpose, risks and benefits, and describes what is involved in the study. It also tells you what other choices you have.

Up to 40 people will be in the phase I and phase II portions of the study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for further information. There is no guarantee that this procedure will be successful.

Even if you join this study, you may stop at any time. There is no penalty for stopping. If you decide not to be part of this study, you will continue receiving medical care. If you would like to be part of this study, we will ask you to sign this form. You will get a copy to keep.

Why is this study being done?

Sometimes it is difficult to find a "matched donor" in the family (related donor) or in the Bone Marrow Registry (unrelated donor). When this happens, we may choose a donor who is only partially matched to you. This can sometimes cause problems, such as graft rejection (when the body rejects the new cells), graft-versus-host disease (GVHD) (when the new cells attack the body), or even death. Therefore, there is a great need to develop safer and more effective protocols when using mismatched donors.

To address these problems, we will test a *nonmyeloablative* transplant from a *haploidentical* donor.

- Unlike a standard transplant, a *nonmyeloablative transplant* uses milder or lower doses of drugs or radiation to leave some of the immune system intact. Drugs help your body accept the new donor cells.
- A *haploidentical donor* is related to the patient, but has a different tissue type. This tissue type is matched by at least 50% to the patient. A haploidentical transplant is considered an "alternative" transplant to traditional methods.

As compared to conventional transplants with matched related and unrelated donors, haploidentical transplants have been associated with a higher risk of:

- GVHD
- Infections.
- Relapse after transplant.
- Rejection of the new bone marrow.

This trial is asking whether the addition of extra cells from the same haploidentical donor one week after transplant can help prevent these problems. These cells are known as *natural killer cells* or *NK cells*. The addition of NK cells is considered *investigational therapy*.

- *NK cells* are a type of white blood cell.
- They have been shown to fight infections and fight cancer cells.
- They have been shown to help new bone marrow stem cells engraft.

When we do the transplant followed by an infusion of donor NK cells, we will want to find out:

- Are adding *NK cells* after *non-myeloablative, haploidentical* transplant safe?
- Will these *NK cells* reduce the rates of relapse and graft rejection?
- Will these *NK cells* help fight infections after transplant?

Hospitalization

Pediatric patients (those under 18 years of age) may require hospitalization for this treatment. All of the research studies will be done in the hospital. You will be discharged to the outpatient department when the inpatient doctor decides you are ready. You may need hospitalization at other times if you get sick.

Adult patients (those 18 years of age and older) the treatment, including infusion of donor bone marrow cells and NK cells, can be done as an outpatient. You may get hospitalized at other times if you get sick.

Procedures that will be done as part of the transplantation

Conditioning:

You will get drugs and radiation to suppress the immune system and destroy the abnormal marrow, so the donor's healthy cells can grow and produce new blood cells. This is called "conditioning." You will get these drugs through the central venous catheter:

- *Cyclophosphamide*: 2 doses total, on days −6 and −5.
- *Fludarabine*: 1 dose per day for 5 days (day −6 through day −2.).
- *Total Body Irradiation*: The day before the transplant, you will get 1 dose of radiation. (If the patient is too young to be still, anesthesia will be provided.)

You will also get medications to help prevent nausea and vomiting.

Bone marrow transplant:

The donor's bone marrow stem cells will be given through the central venous catheter, similar to a blood transfusion. From these stem cells will grow the components found in blood: red blood cells that carry oxygen, white blood cells that fight infections, and platelets that make clots.

Post-transplant immunosuppression:

Starting on day 3 after the transplant, we will give you strong immune suppressing drugs. The purpose of these drugs is to allow the new bone marrow cells to be accepted and to try to reduce the risk of GVHD.

The drugs are:

- *Cyclophosphamide:* One dose on day 3 after transplant through the central venous catheter.
- *Mesna:* 4 doses with each dose (1 just before the cyclophosphamide and 3 just after). Mesna is not chemotherapy. It is a medicine that helps protect your bladder from the side effects of high-dose cyclophosphamide.
- *Tacrolimus* twice a day beginning on day 4 until 84 days after the transplant, first by central venous catheter, then by mouth. The dose will then be gradually reduced over a period of 13 more weeks, until day 180.
- *Mycophenolate mofetil (or MMF)*: Three times a day beginning on day 4 until day 40, first by central venous catheter, then by mouth. The dose will then be gradually reduced over a period of 6 more weeks, until day 84.

If you develop GVHD or we think your body may reject the donor cells, you may need to take the drugs for a longer time or we may need to add other drugs.

Post-transplant bone marrow recovery

Starting on day 4 after transplant, we will start granulocyte colony stimulating factor (GCSF) to help the new white blood cells grow. This will be given either as an injection under the skin, or through an IV or central venous catheter. GCSF will continue until enough new white blood cells grow.

Post-transplant donor NK cell infusion

The same haploidentical family member who gave you cells for your bone marrow transplant will also give you cells for your NK cell infusion. One week after transplant, you will receive the NK cells as a single infusion through your central venous catheter.

- You will also have blood tests at least three times a week to check kidney function and blood cell counts early after the transplant
- Other blood tests routinely done include liver function and electrolytes (blood salts).
- In addition, a bone marrow biopsy will be needed at various time points. The bone marrow and blood samples will be evaluated for the presence of donor cells to determine how well you have accepted the new stem cells.
- You will undergo scheduled screening tests to make sure that your cancer has not come back. This screening is specific for your type of cancer. Your doctor can provide more details regarding your screening tests.

Here is the **schedule of conditioning and post-transplant procedures:**

	Days before transplant					
	−6	−5	−4	−3	−2	−1
Conditioning						
Cyclophosphamide	●	●				
Fludarabine	●	●	●	●	●	
TBI						●

	Days after transplant					
	+3	+4	+7	+40	+84	+180
Post-Transplantation						
Cyclophosphamide	●					
Mesna	●					
MMF		Start	→	Taper*	Stop*	
Tacrolimus		Start	→	→	Taper*	Stop*
G-CSF**		Start				
Donor NK Cell Infusion			●			

* We will reduce the dose around this time, depending on your GVHD status.
** Continues until enough new white blood cells grow.

Blood and Bone Marrow Tests for Research

Sample	Sample Size	Timing
Bone marrow aspiration	Up to 2 ml (about ½ teaspoon)	Before transplant, We will try to collect this sample at the same time as your regularly scheduled doctor visits.
Blood	Up to 45 ml (about 3 tablespoons)	Before and after transplant, and after you return home at approximately Day +7, +14, +28, +56, +84, and one year . We will try to collect these samples at the same time as your regularly scheduled doctor visits.

We will use your blood and tissue samples for research to study your immune system recovery. This may involve sending your research samples to outside research labs. Samples will be stored indefinitely.

If we want to use your tissue in the future for a purpose not described in this consent, we must first send a request to the Institutional Review Board (IRB) for review and approval for all proposed new research.

How long will I be in the study?

Your treatment at the SCCA will last about 3½ months, but could be longer. You may be asked to return for follow up at 6 months and every year thereafter, 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 understand the long-term effects of the transplant. But you may be taken off the study and followed less often if:

- The study treatment does not work for your disease;
- 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 disease;
- Other treatments for your disease become available;
- By your request.

What are the side effects (risks)?

<u>Transplant</u>

We expect that the transplant itself will have relatively minor side effects (like a blood transfusion). However, after the transplant you will be at very high risk for complications, including death. The side effects of transplant are related to the chemotherapy, radiation therapy, and immunosuppression that you will be receiving. You may need red blood cell and platelet transfusions and antibiotic therapy.

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 with infusion of marrow and/or NK cells (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	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	Failure of liver function
Infection	Red Blood Cell Destruction	Failure of brain function
Time away from work		Impairment or failure of kidney function
		Failure of lung function
		Bleeding or dysfunction of the central nervous system

NK Cell Infusion

We expect that the NK cell infusion itself will have relatively minor side effects. Potential side effects are listed in the table and all are considered rare (less than 3% of patients, or 1-2 out of 100 patients or less). There may be complications or side effects that we do not know about.

Graft-versus-host disease	Diarrhea
Nausea	Possible allergic reaction (including itching, hives, flushing [red face], shortness of breath, wheezing, chest tightness, skin rash, fever, chills, stiff muscles, or trouble breathing)
Vomiting	
Infection	
Prolonged neutropenia (low white count)	Marrow suppression

There is a very small risk (less than 1%, or 1 out of 200 patients or less) of developing antibodies against proteins that are leftover on the NK cells. This leftover protein is needed to select the NK cells from the donor's blood and is a critical part of the NK cell collection process.

Side effects may occur at the time of transplant or after. They may require hospitalization, medication, or therapy. Risks and side effects vary from person to person. Your doctor may be able to change or give medications to make some of the side effects less bothersome.

Side effects such as GVHD and infections can be very serious, long lasting, and/or life threatening. Please talk with your study 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.

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 pre-existing damage to any organ system. Although the aim of this study is to reduce the risks of having bone marrow transplants, **the side effects of treatment could be severe and include a risk of death**.

There is a risk that your disease will come back, even if the transplant works at first. Also, the transplant may be less successful at treating your disease than a standard stem cell transplant from a matched related donor, and the rate of disease recurrence may be higher.

Rejection of donor cells: There is a risk that you will reject the donor blood stem cells and that the donor cells will not be detected after transplant. Transplants from haploidentical donors are at a higher risk of rejection. If this occurs, we expect your own blood counts to recover. When this happens, you are also at higher risk of relapse if you have a history of leukemia. Rarely, rejection may occur without recovery of cells. This type of rejection can be fatal. It can only be treated by a second stem cell transplant.

Cyclophosphamide is a type of chemotherapy used in stem cell transplants to try and reduce the risk of rejection and/or GVHD.

Likely side effects	Less likely	Rare
Low white blood cell count Low red blood cell count Diarrhea Vomiting Liver damage Lower sperm production in men Hair loss Nausea 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 Darkening of nail beds Fetal damage (if pregnancy occurs while taking cyclophosphamide) Secondary cancers Infertility	Lung scarring (fibrosis) with cough and shortness of breath Heart failure (with high doses) Decrease in sodium level in the blood with high doses

Cyclophosphamide can cause bleeding in your bladder. Getting more fluid through a vein or your catheter and drinking extra liquids may prevent this. If the bleeding becomes severe, the bladder may need to be washed out with a salt-water solution, using a bladder catheter (thin plastic tube).

DO NOT take any aspirin or nonsteroid anti-inflammatory medications (e.g., Ibuprofen, Motrin, Advil). Report easy bruising or bleeding such as a nose bleed, bleeding of gums when you brush your teeth or have black/bloody stools.

Mesna is used to prevent bleeding from the bladder, a possible side effect of cyclophosphamide. It is not chemotherapy.

Likely side effects	Less likely
Nausea Vomiting Diarrhea	Abdominal pain Altered taste Rash Hives Headache Joint or limb pain Low blood pressure Fatigue

Fludarabine is a chemotherapy used to try and reduce the risk of rejection.

Likely side effects	Less likely	Rare
Low white blood cell count with an increased risk of infection (from bacteria, fungi or viruses) Low platelet count with an increased risk of bleeding Anemia	Nausea Diarrhea Fatigue	Vomiting Trouble seeing or problems with your eyes Numbness or tingling in your fingers or toes Confusion or coma Pneumonia Secondary cancers

Total body irradiation (TBI) is "full body" radiation used to help weaken or destroy your abnormal bone marrow cells. The dose used in this protocol will be much lower than that used in standard transplant protocols. TBI may destroy normal bone marrow cells.

Likely side effects	Less likely
Nausea Fatigue	Temporary hair loss Vomiting Diarrhea Painful swelling of the parotid gland (a gland under the chin) for a few days Cataracts (an opacity or whitening of the lens) in the eye Secondary cancers Sterility Major genetic damage to children conceived after transplant Damage to the lungs

Patients receiving radiation have a risk of developing a secondary cancer later in life. 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 very small in comparison to the therapy dose you will receive. They are not expected to increase your health risk.

TBI may also cause damage to the lining of the mouth, called "mucositis" that requires pain medication and temporary administration of fluids and nutrition by vein. TBI may cause diarrhea that lasts for a few days. In addition TBI can cause damage to the lungs and often causes the formation of cataracts many years after its administration.

Tacrolimus is a drug used to treat GVHD. During treatment, we will monitor the levels of tacrolimus in your blood, to see if we need to adjust the dose.

Likely side effects	Less likely	Rare
High blood pressure (hypertension) Shaking of hands (tremor) Changes in liver or kidney function Altered levels of magnesium, calcium, potassium, and sugars in the blood	Headache Pain in the hands or feet. Increases in cholesterol and triglyceride levels Nausea/vomiting Changes in how clearly one can think Trouble sleeping	Patients have had seizures, but it is unclear whether tacrolimus, other drugs, or a combination of drugs were responsible. Renal failure from damage to the blood vessel walls and destruction of red blood cells by a condition called hemolytic uremic syndrome (HUS)

Mycophenolate Mofetil (MMF) is a drug used for suppressing the immune system. It 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 and the coordinating center 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	Rare
Nausea Birth defects	Vomiting Diarrhea and abdominal discomfort Lower red blood cell count that is reversible Lower white blood cell count with increased risk of infection	Stomach bleeding Blood in stools Secondary cancers

Granulocyte Colony Stimulating Factor (known as GCSF, Neupogen, or growth factor) is a drug used to help increase your white blood cell count after transplant.

Likely side effects	Less likely
Muscle aches or pain Bone pain Itching Skin rash Headache	Blood vessel inflammation (vasculitis) Ruptured spleen

Graft-versus-host-disease (GVHD) is a known complication of bone marrow transplantation. It has occurred in 50 - 70% of patients on similar studies. **When you receive stem cells from a donor with a different tissue type than yours, the risk of GVHD is higher**. However, we are hoping to reduce this complication to less than 30% by using cyclophosphamide on day +3 after transplant.

GVHD can occur early after the transplant (called acute GVHD) or late after transplant (called chronic GVHD). In GVHD, donor cells react against cells of your body. GVHD may cause skin damage (rash, discoloration, and tightness); gastrointestinal damage (nausea, vomiting, and diarrhea); liver damage (abnormal liver function tests and jaundice); lung damage, dry mouth or sores of the mouth, dry eyes, weight loss, and hair loss. GVHD may be mild or severe. It may require prolonged treatment (sometimes for years) with immune suppressing drugs to reduce inflammation. **Severe GVHD and complications of its treatment can result in death.**

Side effects of GVHD include:

Acute	Chronic
Skin rash Lack of appetite, stomach cramps, diarrhea or "full" feeling in stomach Intestinal bleeding Problems of the liver Problems of the stomach Nausea Vomiting Death	Eye problems Skin problems Liver problems Problems of the mouth, lips, and throat Lung problems *And all the risks listed under "Acute"*

Early (acute) or late (chronic) GVHD may become so bad that it results in death. GVHD is treated with drugs that weaken the immune system. This makes you more likely to get infections.

A very effective drug for treating GVHD is prednisone, which is a type of steroid. However, prednisone is often required at high doses for 9 months to several years. Depending on the dose and duration of treatment, side effects may include weight gain, depression or psychosis (mood swings), cataracts, diabetes, muscle loss, bone loss or fractures, avascular necrosis (break down) of hip or other joints that may require joint replacement, high blood pressure and others.

Reproductive risks

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 or abstinence for one year after transplant. If you are still on

MMF for more than one year after transplant, you must continue using two forms of birth control until you have been off MMF for at least 2 months. 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. In males who have reached puberty and have received 300 cGy radiation, most men will have return of sperm counts by 30 months. But some men will not recover sperm counts, and sterility can still occur. 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.

Cyclophosphamide can sometimes make it harder to have a baby (infertility). The doses in this study are much lower than in a standard transplant, so your risk of infertility is also lower. Since you will be receiving a combination of both radiation and cyclophosphamide, the risk of infertility or sterility may be higher than receiving each alone.

If you are a male and have reached puberty, you can talk to your doctor about ways of storing sperm. If you are a woman and have reached puberty, egg storage is much more difficult. Talk to your doctor if you are interested in learning more about this.

Other risks

If you have severe side effects, which can include low blood counts, infections, bleeding, and failure of the donor stem cells to grow, you may need red blood cell and platelet transfusions. Red blood cell and platelet transfusions have a very small risk of transmitting serious infections. You may need antibiotics or other medications to treat the side effects.

There is a risk that you might develop a fatal lymphoma, called Post-Transplant Lymphoproliferative Disease (PTLD). The risk of PTLD is small; it has occurred in 5% of patients who were given standard (high-dose) transplant regimens. All these patients had either a diagnosed immune deficiency before the transplant, or severe GVHD after transplant that required intensive immune suppressive therapy. If you have either of these risk factors you may be at risk for development of PTLD.

Are there benefits to taking part in this study?

There may or may not be direct medical benefits to patients in this study. We hope that this treatment will result in a cure of your bone marrow failure or leukemia and help your immune system function better after transplant. Some patients may not directly benefit, but may be encouraged by knowing that being in this study may help future patients with the same disease.

What other treatment options are there?

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

- Treatments that help with the symptoms of your disease. These may include antibiotics, blood transfusions, enzyme replacement, special diets, as well as other standard medical treatments.
- Treatments that are considered experimental. For example, some patients may be eligible for gene therapy or other experimental forms of stem cell transplant.

- A conventional stem cell transplant, which uses higher doses of chemotherapy and radiation therapy.
- Waiting for a bone marrow donor who has a better tissue match to you.
- No treatment.
- Comfort care.

Before you agree to this study, please talk with your doctor about these and other options that may become available.

Will my medical information be kept private?

The individuals responsible for this study will try to keep your personal information as private as possible and ensure that it is disclosed only in accordance with state and federal law and the terms of this consent. However, it is not possible to guarantee absolute privacy. In addition to disclosures in accordance with state and federal law, the organizations that are listed below may inspect or copy your research records for quality assurance and data analysis. Your research records will identify you by a unique patient number (UPN) that may be linked to your name and will include things such as your medical record, medical history, results of your blood tests and exams, reports from your treatment, and reports of your office visits. For any published reports, a different coding system not linked to your name will be used.

Who has access to my research record information?

You will receive some services, tests, or procedures at University of Washington clinical facilities ("UW Medicine") and/or at the Seattle Cancer Care Alliance ("SCCA") as part of this study. This means that information about this study will become part of your medical record. If you do not already have a UW Medicine or SCCA medical record for clinical purposes, one will be created for you. Basic information such as the name and number of the study, the study sponsor, the names and contact information of the study staff will be included in your medical record.

Research procedures and test results may also be put in your medical record. This will include things such as your medical history, results of your blood tests and exams, reports from your surgery and treatment, reports of your office visits.

If you have already given or in the future decide to give permission to any person or group (such as an insurance company or employer) to have access to your medical record, the information about this study and your participation in it will be included. This could affect your ability to get life insurance or a new job.

It is important for you to consider the possible risks of including study information in your medical record before you sign this consent form.

We will try to keep your personal information as private as we can. We cannot guarantee absolute privacy. Your personal information may be disclosed if required by law. Some people may see or copy your medical records. They would do this as part of their research, to make sure this study is being done correctly and safely, or to evaluate the results. Organizations that may inspect and/or copy your research records for quality assurance and data analysis include the groups listed below.

- Researchers involved with this study
- Fred Hutchinson Cancer Research Center (FHCRC), University of Washington (UW), Seattle Children's, and Seattle Cancer Care Alliance (SCCA)
- Medical College of Wisconsin
- US Food and Drug Administration (FDA), National Institutes of Health (NIH), and Office for Human Research Protections (OHRP)

- Institutional Review Boards (IRB) (groups who review the study to protect your rights as a research participant)
- Miltenyi Biotec

What are the costs of taking part in this study?

Miltenyi Biotec will cover the cost of the reagents used to select the NK cells from your donor's cells collected post transplant on day 7. Research funding will provide the remainder of the laboratory costs of the NK cell selection. You or your insurance company will pay the rest of the medical expenses relating to, or arising from, this study. 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 SCCA Patient Financial Services Department at (206) 288-1113.

Will I be paid to take part in this research study?

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

Do I have to be part of the study?

Joining this study is up to you. You are free to say yes or no, or to drop out after joining.

However, stopping treatment during conditioning or after the transplant could have very serious health consequences, even death. Stopping MMF and tacrolimus after the transplant could lead to rejection of the donor stem cells, or to life-threatening GVHD. If you are thinking about dropping out of this study, please tell your doctor and the study doctor.

What are my rights as a study participant?

- You do not have to join this study. You are free to say yes or no. Your regular medical care will not change.
- If you join this study, you do not have to stay in it. You may stop at any time (even before you start). There is no penalty for stopping. Your regular medical care will not change.
- 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 may learn new information you need to know. For example, some information may affect your health or well-being. Other information may make you change your mind about being in this study. If we learn these kinds of information, we will tell you.

For more information

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

For Questions About	Please Contact
This study and what it involves	Your doctor (attending physician) or one of the investigators listed at the beginning of the consent
Your rights as a participant in a research study	Karen Hansen, in the Institutional Review Office, FHCRC at 206-667-4867
Your bills and health insurance coverage	Seattle Cancer Care Alliance, Patient Financial Services at 206-288-1113
Research use of your blood or tissue sample, or research files	Clinical Research Division, Data Management Office, FHCRC/Clinical Research Division at 206-667-4728
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; Seattle Children's(206) 987-2032
Medical records?	Contact the Seattle Cancer Care Alliance's Director of Health Information Management at 206-288-2174.

Signature

Before you sign this consent form, make sure of the following:

- You have read this consent form, or someone has read it to you.
- This study has been explained to you.
- You had the chance to ask as many questions as you wanted.
- You understand you can ask more questions anytime.
- You understand you (or your insurer) will have to pay the costs of being in this study, including treatment for side effects.
- You understand your medical records will be available to the doctors, staff, and other groups working on this study.
- You agree to join this study.

Participant (age 14+) / date

Parent or legal guardian (for participants under 18 years) / date

Other parent or legal guardian (if reasonably available) / date

Medical Staff Person's Statement

I have discussed the above research study, including the study procedures and possible alternatives and risks, with the person signing above. I encouraged questions and have answered them to the best of my ability. A copy of the signed consent form will be given to the participant.

Medical Staff Person's Signature

Date

Printed Name and Title of Medical Staff Person

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

2230.00A – Current version: 04/14/2016
Previous version: 12/09/2014
Copies: Patient, Medical Records, Research File

Signed Consent <u>MUST</u> be sent to Data Management –
LF-229FHCRC, 1100 Fairview Avenue North, Seattle, WA 98109-1024