FRED HUTCHINSON CANCER RESEARCH CENTER
UNIVERSITY OF WASHINGTON SCHOOL OF MEDICINE
SEATTLE CHILDREN'S

Consent to Participate in:

Transplantation of Umbilical Cord Blood for Patients with Hematological Diseases with Cyclophosphamide/Fludarabine/Total Body Irradiation or Cyclophosphamide/Fludarabine/Thiotepa/Total Body Irradiation Myeloablative Preparative Regimen (Protocol 2010)

Consent Form for Regimen B: Middle Intensity Regimen (Cyclophosphamide/Fludarabine/Thiotepa/Total Body Irradiation)

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.

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Emergency (24 hour) Phone (For Children): (206) 987-2032; Fax (206) 987-2764

We would like you to join this research study.

To help you decide if you want to join this study, you should:

- Read this form.
- Ask your doctor or nurse questions about this study.
- Have your doctor or nurse explain anything you do not understand.
- Talk with your family or friends about joining.
- Take time to think about joining.

After you have learned about this study, met with your doctor and asked questions, you can decide if you want to join this study or not. This process is called **informed consent**.

This **informed consent** form gives information to help you decide if you want to join this study or not. In this form, we explain why we are doing this study, the risks and benefits to you, your choices, and other important information. Your doctor will explain the research study to you.

If you decide to join this study, we will ask you to sign this form. After you sign the form, you will get a copy to keep.

The purpose of a research study is to answer questions.

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

We are inviting you to join this study because you are eligible for a cord blood transplant. The purpose of this study is to examine how patients respond to a cord blood transplant after doses of chemotherapy and radiation by collecting data throughout the transplant process, specifically looking to see if the disease is absent or present at six months, one year, and two-years post-transplant. Information we learn from larger numbers of patients will allow us to make more accurate estimates about these outcomes.

You do not have to be in this study.

Joining this study is up to you. You are free to say yes or no. Your regular medical care will not change. Even if you join this study, you do not have to stay in it. You may stop at any time. There is no penalty for stopping, and your regular medical care will not change.

Background

Blood stem cells are the “parent cells” of the blood and bone marrow. They grow inside your bone marrow, which is your body’s “factory” to make the cells that circulate in your blood. These include: red blood cells (which carry oxygen), white blood cells (which fight infection), and platelets (which prevent bleeding). Certain cancers can be treated by giving patients stem cells that come from someone else. This is called a stem cell transplant. As part of the transplant process, patients receive doses of chemotherapy and radiation to treat their underlying disease, such as cancer. As one of its effects, this treatment also kills the healthy blood stem cells that are already in the bone marrow and giving a patient blood stem cells from a healthy donor leads to recovery of the bone marrow and provides a new blood system that makes the cells that circulate in the blood. In the case of this study these new blood stem cells will come from umbilical cord blood.

Cord blood transplants are relatively new, and we’re striving to make them even more safe and effective in the future. We do most transplants as part of a study; which means that we follow a detailed protocol to make sure it’s always done the same way and we keep careful records so that we can evaluate the outcomes. Therefore, we would like to transplant you on this research study and collect information about the outcome of your transplant. Analysis of the outcomes of these transplants will help us improve transplant outcomes in the future.

How many people will take part in the study?

Approximately 135 patients will be enrolled in this study.

What research tests, procedures, and treatments are parts of this study?

This research program involves the use of the following drugs, treatment programs, or research procedures:

Cyclophosphamide
Fludarabine
Thiotepa
Total Body Irradiation
Cyclosporine A
Mycophenolate mofetil
GCSF
Cord Blood Stem Cells

Conditioning (pre-transplant chemotherapy and radiation)

You will be receiving the Middle Intensity Regimen. The conditioning regimen is standard treatment and is not experimental. It will involve the following:

- Six days before the transplant, you will be admitted to the hospital on the bone marrow transplant unit. You will also need a central venous catheter for transplant, so if you do not already have one, one will be placed.

- Chemotherapy (fludarabine and thiotepa and cyclophosphamide) and TBI are given with the intent of helping to kill cancer cells and to prepare your body for the cord blood stem cells by suppressing your immune system. These procedures are described in a table below.

Middle Intensity Regimen (TBI total 400 cGy (200 cGy/day x 2 days, -2 to -1))		
Day	**Conditioning**	**Supportive Care/Other**
6 days prior to transplant	Fludarabine Cyclophosphamide	
5 days prior to transplant	Fludarabine Thiotepa	
4 days prior to transplant	Fludarabine Thiotepa	
3 days prior to transplant	Fludarabine and begin CSA (100+ days)	
2 days prior to transplant	Fludarabine TBI once daily	
1 days prior to transplant	TBI once daily	
0 (TRANSPLANT DAY)	Unmanipulated cord blood unit(s)	Begin MMF
1 day after transplant		Begin GCSF (daily until recovery of white blood cell count)

Transplant Day

On Day 0, the transplant day, the cord blood stem cells are given intravenously through the central venous catheter.

Immunosuppression Therapy

As part of the transplant procedure, you will be given two drugs to reduce the risk of graft versus host disease, a complication that occurs when the cord blood stem cells recognize the patient's body as foreign and attack it. These drugs will be started three days before the cord blood stem cells are given. Both drugs will initially be given through your central venous catheter and then changed to a pill form when you can take a capsule orally as tolerated. The first drug is called Cyclosporine A. Cyclosporine will be continued for at least 100 days and most probably until Day 180 after transplant. The second drug is called Mycophenolate Mofetil (MMF). MMF will continue for at least 30 days.

Follow-up

To speed the recovery of blood cells as much as possible, you will receive granulocyte-colony-stimulating factor (GCSF or Neupogen). GCSF signals the bone marrow to make white blood cells, which are needed to fight and prevent infections. You will start receiving GCSF through your central line or as an injection under the skin the day after transplant. You will continue to receive it daily until your white blood cell count recovers.

In order to evaluate how your new marrow is developing, you will have blood drawn and/or bone marrow biopsies at specific time points. You are planned to have blood drawn at Day 28, Day 56, Day 80, 6 months, 1 year and 2 years after your transplant.

You will be discharged from the inpatient bone marrow transplant unit when you are ready to be cared for as an outpatient. Initially, it will be necessary for you to have frequent visits at the outpatient transplant clinic, and then at specific times as determined by your physician.

You will be followed in the study for 2 years. After you have recovered from any immediate transplant related complications, follow-up will be routine and according to your specific disease type, but we will continue to collect data on how your marrow is functioning at these follow-up visits.

As part of follow-up, we would like to contact you and/or your referring physician around 6 months, 1 year, and 2 years after transplant to see how you are doing. We may contact your physician to request copies of blood test results and other tests and procedures done as standard post-transplant follow-up. This will help us learn about the long-term effects of the study.

How long will I be in the study?

You will be followed in the study for 2 years. Even after you are discharged from the transplant center, we will work with your health care provider to gather information about your general health status and transplant-related problems for up to 2 years.

As part of follow up, we would like to call you on the telephone around 6 months and two years after transplant to see how you are doing. Keeping in touch with you and checking on your condition at these times helps us look at the long-term effects of the study.

The researcher may stop you from taking part in this study at any time if he/she believes it is in your best interest; if you do not follow the study rules; or if the study is stopped.

You can decide to stop at any time. It is important to tell the study doctor if you are thinking about stopping so any risks from the treatment can be evaluated by your doctor. Another reason is to discuss what follow-up care and testing could be most helpful for you.

What side effects or risks can I expect from being in the study?

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

Risks Associated with Conditioning, Immunosuppression and Supportive Therapies

1. Cyclophosphamide (Cytoxan):

Likely Side Effects	Less Likely Side Effects	Rare Side Effects
• Lower white blood cell count with increased risk of infection • Diarrhea (loose stools) • Vomiting (throwing up) • Liver damage • Lower sperm production in men • Hair loss • Nausea (feeling sick to your stomach) • 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 • 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.

2. Fludarabine:

Likely Side Effects	Less Likely Side Effects	Rare Side Effects
• 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	• 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 • Severe problems with your brain (confusion or coma) • Pneumonia

3. Mycophenolate Mofetil (MMF):

Likely Side Effects	Less Likely Side Effects	Rare Side Effects
• Nausea (feeling sick to stomach) • Miscarriage or birth defects if become pregnant while taking and within 6 weeks after stopping MMF	• 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 • Progressive multifocal leukoencephalopathy (a serious brain infection that can cause weakness, clumsiness and confusion and can lead to death)

4. Cyclosporine:

Likely Side Effects	Less Likely Side Effects	Rare Side Effects
• Nausea (feeling sick to your stomach) • Vomiting (throwing up) • Loss of magnesium, calcium, potassium • Hypertension (high blood pressure) • Tremor (shaking of the hands) • Increased hair growth	• Pain in the hands and/or feet. The pain decreases or goes away with the improvement of graft-versus-host disease (GVHD), with a decrease in the rate of infusion, or when the cyclosporine is switched from the intravenous (by vein) to the oral form. • Blood test results that show changes in the liver or kidney (the dose will be lowered or even stopped). • Increases in cholesterol and triglyceride • Changes in how clearly one can think	• Patients have had seizures, but it is unclear whether cyclosporine, other drugs, or a combination of drugs were responsible. • Secondary cancers

5. Thiotepa

Likely (Over 10%)	Less Likely (1-10%)	Rare (Less than 1%)
• Low white blood cell count with an increased risk of infection (from bacteria, fungi or viruses) • Low platelet count with increased risk of bleeding • Anemia • Nausea/vomiting • Diarrhea • Anorexia (loss of appetite) • Mouth ulcers • Sores in mouth or on lips • Missing or stopping of menstrual periods in women	• Skin rash • Change in skin coloring • Fatigue, weakness • Dizziness • Headache • Permanent sterility (inability to have children)	• Allergic reactions during infusion (fever, chills, itching, hives, flushing, rash, shortness of breath, wheezing, chest tightness, muscle stiffening) • Confusion • Seizures • Liver damage • Secondary cancers

6. Total body irradiation (TBI):

Likely Side Effects	Less Likely Side Effects
• Nausea (feeling sick to stomach) • Fatigue (feeling tired) • The irradiation dose used will probably result in sterility	• 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

You will also have tests such as CT scans and chest x-rays, based on medical necessity and to help follow your progress. These studies are routine care after a 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.

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 bone marrow transplant begins to work. Blood transfusions are given as needed.

7. Granulocyte Colony Stimulating Factor (GCSF):

Problems we anticipate to be common:	Problems we anticipate to be less common:	Problems we anticipate to be infrequently encountered:
	▪ Ache or pain inside the bones, increased levels of liver enzymes and uric acid in the blood, low number of platelets in the blood	▪ Allergic reaction, low fever ▪ Enlargement of the spleen and even splenic rupture ▪ Worsening of pre-existing skin rashes, ▪ Hair loss ▪ Inflammation of a blood vessel in the skin

The above tables list the side effects of the drugs individually; however, when used in combination (as they will be here for pre-transplant chemotherapy/radiation), there may be an increase in the occurrence of some side effects. For example, sores in the mouth (mucositis) are likely with this combination (cyclophosphamide, fludarabine and TBI) and may be severe.

8. Late Complications:

- 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 Associated with Cord Blood Transplantation

The following problems may occur as a result of the transplantation of umbilical cord blood. These are risks that would be present whether such a transplant was done as part of a research study or not.

1. **Infusion Side Effects (occurring from time of infusion to 2 days after):** Cord blood cells are stored in a solution containing dimethyl sulfoxide (DMSO) to protect the cells during freezing. The following side effects may occur with infusion:

Likely (Over 10% of patients)	Rare Side Effects (Less than 1%)
• Unusual taste in the mouth • Unpleasant odor from the lungs (and breath) for a few days after getting the stem cells • Temporary rise in blood pressure • Nausea, vomiting • Blood in urine • Anxiety	• Itching • Hives • Rash • Shortness of breath • Wheezing, chest tightness • Drop in oxygen levels • Changes in heart rate, rhythm or function • Fever • Chills • Sweating • Headache • Stiff muscles • Kidney failure

2. **Slow bone marrow recovery:** Blood counts, including red blood cells, white blood cells, and platelets, may be very slow to recover after unrelated donor umbilical cord blood transplantation. Until the new cord blood stem cells begin to grow, you are at risk of developing infections or bleeding. Infections can be treated with antibiotics but sometimes can be very serious. Bleeding can be corrected, at least in part, by transfusions. However, there are risks associated with the transfusion of red blood cells and platelets during the post-transplantation period. These risks include serious allergic reactions and infections, including hepatitis, cytomegalovirus (CMV), and human immunodeficiency virus (HIV; the virus that causes AIDS). All blood products, however, will be screened for these infections in order to reduce the chance that the blood contains these viruses.

3. **Graft failure:** The cord blood stem cells may fail to “take” or engraft. Past experience suggests that this may occur in about 10% of patients overall. It is possible that the cord blood stem cells will grow, but not work normally. This will result in low blood counts for a long period of time. Graft failure is typically fatal in traditional transplants and may be fatal in this type of transplant also. Should the graft fail, you will not have access to additional stem cells from the same infant donor; instead, you may be able to receive a second transplant with stem cells from another unrelated umbilical cord blood donor or a mismatched parent or sibling (i.e., brother or sister) donor.

4. **Graft versus host disease (GVHD):** This condition results from a reaction of the transplanted umbilical cord blood cells against your body and organs. This reaction ranges from a mild skin disorder to severe involvement of the skin, liver or gut. It may be fatal in some patients. You will be monitored closely for this complication and given specific treatment to prevent and treat it. There are 2 forms: acute (early) and chronic (late) GVHD.

Acute GVHD may produce skin rashes, liver disease, diarrhea, and an increased risk of infection. All of these can range in severity from mild to fatal. To confirm the diagnosis of acute GVHD, you may be asked to have a skin biopsy (i.e., taking a piece of tissue to make the diagnosis of GVHD) and possibly a liver or gut biopsy. The treatment of acute GVHD may require you to take high doses of methylprednisolone or prednisone and, in some cases, other drugs such as anti-thymocyte globulin (ATG).

Chronic GVHD may produce skin rashes, hair loss, thickened skin, dry eyes, dry mouth, liver disease, diarrhea and an increased risk of infection. Chronic GVHD may be mild and respond to agents that suppress the immune system, or it could be very severe; it may also last for several years.

5. **Genetic Disease Transmission:** It is very rare, but there is the potential that genetic diseases (such as thalassemia or Gaucher's disease) may be passed to you through the transplanted cord blood 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 is 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 cord blood stem cells).

6. **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.

7. **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:

   A. **Damage to the vital organs in your body:** This could result in malfunction of any organ in your body such as heart, lungs, liver, gut, kidneys and bladder, brain etc. The lungs and the liver are the most vulnerable. Some patients will experience severe lung problems due to infections and/or due to a reaction of the lungs to the chemotherapy and/or radiation. Some patients can suffer veno-occlusive disease of the liver (VOD) also due to the chemotherapy and/or radiation. Patients who have VOD become jaundiced (yellowish skin), have liver function abnormalities, abdominal swelling, and abdominal pain. Although many patients recover completely, these complications may result in organ failure and permanent damage or even death.

   B. **Serious infections:** Full and complete recovery of your immune system may take many months following the initial recovery of your white cell count. 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 have one of those infections you may have to stay in the hospital longer or be re-hospitalized after transplant. Infections can be fatal. The data collected from several transplant centers indicate that patients who have been exposed to a virus called cytomegalovirus ("CMV") prior to their cord blood transplant are at high risk of

reactivating this virus after the transplant. CMV is a very common virus, similar to the chickenpox virus, that about 50 to 80% of people have been exposed to at some time in their life. In healthy people, the virus remains inactive and does not cause any harm. However, it often becomes reactivated in people with a weakened immune system, and it can cause serious disease in the lungs, digestive tract and other organs. Because we are concerned that cord blood transplant patients are at higher risk for reactivation of CMV, all cord blood transplant patients will be monitored very closely with a special blood test that can detect very early reactivation of CMV. If positive, you will be given appropriate treatments to control the virus. This treatment can last for a long period of time in some patients.

C. **Recurrence of disease:** Your disease may recur even if the transplant is initially successful.

D. **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.

E. **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.

F. **Central venous catheter:** There has been considerable experience with central venous catheter use. The most common complications are clotting and local infection which sometimes 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 re-inflate the lung may be required. There are no long-term effects once the lung puncture has resolved.

Are there Benefits to Taking Part in the Study?

There may be no direct benefit to participation in this study, although we hope that this treatment may control and possibly even cure your cancer with reduced side effects.

Alternative Treatments:

Ongoing conventional chemotherapy may be considered as an alternative to transplantation in treatment of your cancer or bone marrow problem. No further treatment, or comfort care only are also possible alternatives.

Protecting your privacy

Some people may see and/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. These people include the following individuals and organizations:

- Fred Hutchinson Cancer Research Center (FHCRC)
- University of Washington (UW)
- Seattle Children's
- Seattle Cancer Care Alliance (SCCA)
- National Institutes of Health (NIH)
- U.S. Office for Human Research Protections (OHRP)
- Center for International Blood and Marrow Transplant Research (CIBMTR)
- U.S. Food and Drug Administration (FDA)
- Cord Blood Bank (that provided the units for your transplant)
- Institutional Review Boards (IRB)
- Nohla Therapeutics and their agents. Nohla is a company that is collaborating with FHCRC on this study

These people are interested in study data, not your personal information. Personal information is information that can identify you. It may include your name, date of birth, social security number, phone number, or other information.

Study records will be maintained indefinitely for the purpose of analysis and follow-up. We will do our best to keep the personal information in your medical record confidential. But we cannot guarantee total confidentiality. Your personal information may be given out if required by law.

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

Information about your participation in this study (including a copy of this consent form) will be made part of your permanent medical record. If you authorize others to see your medical record, they will see a copy of this consent form.

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.

This research is covered by a Certificate of Confidentiality from the U.S. government. This Certificate helps protect the confidentiality of information about people who join the 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 the funding agency and 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 participants might harm themselves or others.

Costs:

All medical expenses relating to, or arising from, these procedures will be paid by you and/or your insurance company. Taking part in this study may lead to added costs to you or your insurance company. Please ask about any expected added costs or insurance problems.

If you have any questions concerning your financial responsibilities, then contact your financial advisor at the SCCA (206-606-1113).

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this web site. Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

What happens if I am injured because I took part in 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. Ann Dahlberg. She 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.

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

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

Oversight and Review of Protocol Safety:

The FHCRC has guidelines for keeping patients safe in studies. There is a plan for reporting any event that may harm people in a study. The principal investigator, Ann Dahlberg, MD, will make sure this plan is followed.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No

matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution. In the case of injury resulting from 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. Other information may make you change your mind about being in the study. If we learn these kinds of information, we will tell you.

Who can answer my questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor, Ann Dahlberg, MD, at 206-667-1959.

If you have any questions about your rights as a research participant, contact 206-667-5900 or email irodirector@fredhutch.org (Director of Institutional Review Office at Fred Hutchinson Cancer Research Center).

Where can I get more information?

You may call the National Cancer Institute's **Cancer Information Service** at **1–800–4–CANCER (1–800–422–6237)** or **TTY: 1–800–332–8615**
You may also visit the NCI Web site at http://cancer.gov/

- For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials/
- For NCI's general information about cancer, go to http://cancer.gov/cancerinfo/

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/Legal Guardian Date
(for participants under 18 years old)

Other Parent/Legal Guardian / Date
(if reasonably available)

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

Copies to: Participant, Medical Records, Research File

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 signed and dated copy of the consent form will be given to the participant.

_____

Staff Signature Printed Name of Staff Date

Current Version Date: 6/21/2021
Previous Version Date: 8/20/2019