Official Title:	Infusion of off-the-shelf ex vivo expanded cryopreserved progenitor cells to facilitate the engraftment of a single CCR5Δ32 homozygous or heterozygous cord blood unit in patients with HIV and hematological malignancies
NCT Number:	NCT04083170
Document Type:	Informed Consent Form
Date of the Document:	09.28.2022

Fred Hutchinson Cancer Center
University of Washington
Seattle Children's Hospital

Consent to take part in a research study:
Infusion of off-the-shelf ex vivo expanded cryopreserved progenitor cells to facilitate the engraftment of a single CCR5Δ32 homozygous or heterozygous cord blood unit in patients with HIV and hematological malignancies

Local Principal Investigator:
Filippo Milano, MD, PhD, Associate Professor,
Fred Hutchinson Cancer Center. 206-667-5925

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

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

Important things to know about this study.

You are invited to participate in a research study. The purpose of this study is to find out whether it is safe and effective to give patients with both a hematologic malignancy (cancer that affects blood, bone marrow and lymph nodes) and HIV (human immunodeficiency virus) infection one unit of cord blood followed by a unit of the off-the-shelf product (dilanubicel or expanded cord blood cells) in stem cell transplant. This research also aims to look at what happens to the HIV cells in your body in cord blood stem cell transplantation.

The only well-established cure of HIV was in an individual (the Berlin patient) who received hematopoietic stem cell transplant from an unrelated adult donor who had a rare genetic mutation known as CCR5Δ32 that protects from HIV infection. Due to the rarity of finding a matched adult donor carrying the mutation, we will use a cord blood unit prescreened at a cord blood bank for CCR5Δ32 mutation. It is possible that use of this cord blood product to treat your hematologic malignancy may also improve or cure your HIV.

Taking part in this study does not require you to discontinue your current highly active antiretroviral therapy (HAART) and other studies have shown no elevated risk of continuing HAART through transplant. If you and your clinical care provider choose to discontinue HAART post-transplant, the study will follow you to collect clinical information to better understand the effects of this therapy.

You may not benefit from being in this study. Knowledge that we may gain from this study may benefit others. Your participation in this study is completely voluntary. You do not have to participate in this study. You can choose to receive standard methods of stem cell transplant instead of participating in this study. We will give you details about the purposes, procedures, risks and possible benefits related to this study. We will explain other treatment choices available to you, and your rights as a participant in this study.

Please read this consent form carefully. Please ask the study staff questions about anything that you do not understand in this consent form or any questions that you have

that will help you decide whether to join the study. If you choose to join this study, we will give you a signed copy of this form to keep for future reference.

We invite you to join this research study.

We invite you to join this research study because you have been diagnosed with a hematologic malignancy and HIV and are eligible for a cord blood transplant. Up to 10 people will join this study. Doctors at the Fred Hutchinson Cancer Center (Fred Hutch), University of Washington, Seattle Children's Hospital, Case Western Reserve University Hospitals, Children's National Medical Center, and the University of California San Francisco are conducting this research study. The Fred Hutch is the main center for this research study.

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

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

Why are we doing this study?

In this study, we want to learn what side effects, good or bad, dilanubicel has on people with hematologic malignancy and HIV. If you join this study, we would give you dilanubicel and watch carefully for any side effects.

Cord blood stem cell transplant is a standard therapy in many transplant hospitals around the world. Previous experience with cord blood stem cell transplant has led to extended disease-free survival or cure for some patients with hematologic malignancies.

One disadvantage of cord blood transplant is that it takes longer for blood counts to recover in patients treated with cord blood than for patients who receive other types of transplant. Studies have shown that this is because of the small number of cells ("cell dose") in one unit of cord blood. The most common way to give a patient more cells is to use two units of cord blood. This has been done since 2000 and has been shown to improve the survival of cord blood transplant patients.

Even with the use of two units of cord blood, studies have shown that it takes longer for cord blood transplant patients to recover blood counts than in patients receiving other types of transplant. When blood counts are very low for a long period of time, there is an increased risk of bleeding and infection. This may lead to more time in the hospital, and for some people the complications may be fatal.

In a laboratory at Fred Hutch, researchers have developed a way of growing or "expanding" the number of cord blood cells in the lab to provide a temporary source of cells (especially neutrophils, white blood cells that fight infection) while patients are waiting to recover their blood counts after cord blood transplant. The expanded cells are called dilanubicel. dilanubicel is still being studied and government agencies, such as the U.S. Food and Drug Administration (FDA), do not allow this therapy as a standard of care treatment and it can only be used as part of a research study.

We have completed one study using dilanubicel with cord blood transplant at Fred Hutch. Fifteen patients received dilanubicel along with unexpanded cord blood. This was mainly a safety study and there were no safety problems reported. Researchers also compared time to blood count recovery ("engraftment") with a group of patients receiving cord blood transplant without dilanubicel, and the patients who received dilanubicel recovered their neutrophils and platelets (blood cells that prevent bleeding by helping the blood to clot) more quickly than those who did not receive dilanubicel. A larger multicenter study is ongoing to study whether the results from the first study can be repeated with more patients, and 160 patients have received dilanubicel in that study.

Patients in the studies described above received either one or two cord blood units depending on their weight and the cell dose of the unexpanded cord blood. In this study, all patients will receive a single unexpanded cord blood unit with an infusion of dilanubicel. The main question is whether a single cord blood unit is enough for engraftment when combined with dilanubicel in patients with a hematologic malignancy and HIV.

Dilanubicel is made ahead of time and then frozen for use and can be used for any patient without need for matching with the patient's HLA type. A person's HLA type is a set of proteins on the cells that help the immune system to recognize "self" from "other" (like bacteria or viruses). It is possible to use dilanubicel without HLA matching because the immune cells (T cells) in cord blood that could react against the patient are removed before the expanded cells are made.

The unexpanded cord blood unit will be selected for patients as usual for cord blood transplant.

We are also interested in looking at what happens to your HIV infection after cord blood transplantation. Since there haven't been many studies that include patients with both a hematologic malignancy and HIV infection, we hope that the cord blood transplant will potentially control the hematologic disease while also eliminating the HIV cells in your body.

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

Most of the tests, procedures, and treatments you will have in this study are part of the standard care for your disease. However, there are some extra blood tests and procedures you will need to have if you participate in this study. Before any study-related tests and procedures are performed, you will be asked to read and sign this consent form. If you have any questions about the tests mentioned in this section, you should ask the study doctor or study staff.

Study visits may happen at the same time as your visits for routine care either while you are in the hospital or coming into the clinic for scheduled appointments.

Screening:

Before you begin the study, you will need to have tests and procedures done to see if you can be in this study. Some of these procedures would be done for your routine care whether you participate in this study or not.

- Medical history and physical exam
- Disease staging, which may include a bone marrow aspirate and/or biopsy

- MUGA or ECHO to look at your heart function
- Pulmonary function tests
- Pregnancy test
- Blood tests for safety including complete blood counts, blood chemistry (kidney and liver function), panel reactive antibody
- Blood tests for research (prior to conditioning)

If you meet all study requirements and choose to take part, you will be allowed to participate in this study.

Conditioning (pre-transplant chemotherapy and radiation):

The day you receive the unexpanded cord blood unit and dilanubicel is considered “Day 0.” Prior to receiving the cord blood unit and dilanubicel, you will undergo “conditioning,” where you will receive chemotherapy and radiation.

There are two types of conditioning regimens used in this study: high intensity regimen and middle intensity regimen. The type of transplant conditioning regimen you receive will be chosen by your doctor and will depend on your age, details of your disease, and your overall health. These conditioning regimens are standard treatments and are not experimental.

Prior to conditioning, a research blood sample will be obtained. This blood sample will be used to establish a baseline measure prior to receiving dilanubicel.

If you are receiving the High Intensity Regimen, it will involve the following:

- Eight days before the transplant, you will start conditioning. You will be admitted to the hospital on the bone marrow transplant unit. Your doctor will let you know where you will start treatment. You will also need a central venous catheter for transplant, so if you do not already have one, one will be placed.

- Chemotherapy (cyclophosphamide and fludarabine) and total body radiation (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 summarized in a table below.

High Intensity Regimen (High Dose TBI total 1320 cGy (165 cGy BID, total 8 fractions, days -4 to -1))		
Day	**Conditioning**	**Supportive Care/Other**
8 days prior to transplant	Fludarabine	
7 days prior to transplant	Fludarabine Cyclophosphamide	
6 days prior to transplant	Fludarabine Cyclophosphamide	
5 days prior to transplant	Rest	
4 days prior to transplant	TBI twice daily	
3 days prior to transplant	TBI twice daily	Begin CSA
2 days prior to transplant	TBI twice daily	

1 day prior to transplant	TBI twice daily	
0 (TRANSPLANT DAY)	**Unexpanded cord blood unit, followed by dilanubicel**	Begin MMF
1 day after transplant		Begin G-CSF (daily until recovery of white blood cell count)

If you are receiving the Middle Intensity Regimen, it will involve the following:

- Six days before the transplant, you will start conditioning. 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, 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	Begin CSA Begin MMF
2 days prior to transplant	Fludarabine TBI once daily	
1 days prior to transplant	TBI once daily	
0 (TRANSPLANT DAY)	**Unexpanded cord blood unit, followed by dilanubicel**	
1 day after transplant		Begin G-CSF (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. The unmanipulated cord blood unit will be infused first, followed by dilanubicel approximately 4 hours later. The time interval between the two infusions of cells allows us to better follow side effects that might occur with infusion of dilanubicel.

You will receive dilanubicel intravenously (IV; through a vein). The infusion will last about 5-10 minutes. The following procedures will be done several times after the infusion:

- You will be asked how you are feeling and be monitored closely for any side effects from the infusion.
- You will have your vital signs checked, including your heart rate, blood pressure, respiration rate (number of breaths), and temperature.

Immunosuppression Therapy:

As part of the transplant procedure, you will be given two drugs to reduce the risk of graft versus host disease (GVHD), a complication that occurs when the cord blood stem cells recognize the patient's body as foreign and attack it. Both drugs will initially be given through your central venous catheter and then changed to a pill form when you can take medication orally. The first drug is called Cyclosporine A (CSA). CSA will be started three days before the cord blood unit is given (day -3) and continued at full dose for at least 100 days. The second drug is called Mycophenolate Mofetil (MMF). MMF will be started three days before the cord blood unit is given (day -3) or on Day 0 after your cord blood unit infusion, depending on which regimen you receive, and will continue at full dose for at least 30 days.

G-CSF:

To help your blood cells recover as quickly as possible, you will receive granulocyte-colony-stimulating factor (G-CSF or Neupogen). G-CSF signals the bone marrow to make white blood cells, which are needed to fight and prevent infections. You will start receiving G-CSF through your central line or as an injection under the skin the day after transplant (day 1). You will continue to receive it daily until your white blood cell count recovers.

Follow-up:

In order to measure how your new marrow is developing, how your immune system is recovering after your transplant, and how long dilanubicel is in your blood, you will have blood drawn and/or bone marrow biopsies (“chimerism tests”) at specific time points.

Blood draws will be scheduled for Days 28, 80, 6 months, 1 year, and 2 years after your transplant. Bone marrow biopsies are scheduled for Days 28 and 80 and 1-year post-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. Follow-up care beyond Day 80 will be according to your specific type of disease. Your physician will likely want to see you at 6 months, 1 year, and 2 years after the transplant. In addition to the tests mentioned above, your physician may order other procedures or tests based on your diagnosis and your progress after transplant.

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 would you stay in this study?

You will be followed in the study for 2 years.

The study doctor or your doctor may take you out of this study at any time, for any reason, and without your consent. This would happen if:

- They think it is in your best interest not to continue in the study.
- You are unable or unwilling to follow study procedures.
- The whole 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 or decide to stop. He or she will tell you how to stop safely. If you stop the study after receiving the chemotherapy and radiation, but before you receive the cord blood cells, there is a significant increase in the risk of death or life-threatening infection. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

We would like to do long-term follow-up.

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

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

If you choose not to join long-term follow-up, you would not be contacted regularly, and we would not ask your doctor to send medical records, but we might still need to contact you for some other reason.

What are the side effects (risks)?

The side effects associated with transplant can be uncomfortable, and in some cases dangerous, life-threatening, or fatal. Because this is a research study there may be additional side effects which are not known at this time. The known or possible side effects of the treatments you will receive as part of this study are listed below. The risks of the conditioning regimen, immunosuppression and supportive drugs are the same as they would be for a transplant without dilanubicel. If we learn about other side effects, we will tell you.

Risks of Conditioning, Immunosuppression and Supportive Drugs

1. Fludarabine:

Likely (Over 10%)	Less Likely (1-10%)	Rare (Less than 1%)

• Low white blood cell count with increased risk of infection • Low platelet count with increased risk of bleeding • Anemia • Nausea • Vomiting • Diarrhea • Fever • Pain • Cough • Increased risk of unusual infections lasting more than 6 months	• Fatigue • Numbness and tingling in hands or feet • Visual changes • Damage to organs (brain, lungs, others) which may cause tiredness • Changes in thinking or shortness of breath	• Rash • Severe problems with brain (coma at high-doses, confusion) • Pneumonia • Irregular heart beats • Kidney damage which may require dialysis

2. Cyclophosphamide:

Likely (Over 10%)	Less Likely (1-10%)	Rare (Less than 1%)
• Nausea/vomiting • Diarrhea • Loss of appetite • Low white blood cell count with increased risk of infection • Low platelet count with increased risk of bleeding • Sores in mouth or on lips • Fatigue • Blood in urine • Lower sperm production in men • Hair loss • Missing or stopping of menstrual periods in women • Skin changes • Rash • Pain in belly	• Anemia • Liver problems • Damage to the bone marrow (irreversible) which may cause infection • Bleeding • May require transfusions • Allergic reaction • Fluid around heart	• Lung damage • Heart failure with high doses • Liver failure • Secondary cancers • Severe skin rash • Swelling of the body including the brain which may cause dizziness • Confusion

3. 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 • Hair loss	• Skin rash • Change in skin coloring • Fatigue, weakness • Dizziness • Headache • Permanent sterility (inability to have children) • Blurred vision • Blood in urine • Swelling of feet or lower legs	• Allergic reactions during infusion (fever, chills, itching, hives, flushing, rash, shortness of breath, wheezing, chest tightness, muscle stiffening) • Confusion • Seizures • Liver damage • Secondary cancers

4. Total body irradiation (TBI):

Likely (over 10%)	**Less Likely Side Effects (1- 10%)**	**Rare (Less than 1%)**

• Nausea • Fatigue (feeling tired) • The irradiation dose used may result in sterility, and there is a risk of major genetic damage to any children conceived after transplant • Growth failure • Intestinal cramps	• Painful swelling of the parotid gland (a gland under the chin) for a few days • Mucositis • Liver problems • Cataracts (an opacity or whitening of the lens) may develop in the eye • Decreased production of saliva and tear fluid • Decreased function of thyroid gland • Decreased production of other hormones • Temporary hair loss • Vomiting • Diarrhea • Lung damage • Kidney damage • Secondary cancers • Reddening of the skin	• Liver failure • Brain injury • Difficulty swallowing • Vertebral deformities

5. Granulocyte Colony Stimulating Factor (G-CSF):

Likely (Over 10%)	Less Likely (1-10%)
• Muscle aches or pain • Bone pain • Itching • Skin rashes • Headache • Dyspnea (shortness of breath) • Edema (puffiness caused by excess fluid trapped in the body's tissues) • Insomnia	• Blood vessel inflammation (vasculitis) • Ruptured spleen

6. Cyclosporine:

Likely (Over 10%)	Less Likely (1-10%)	Rare (Less than 1%)
• Kidney problems • High blood pressure • Tremor • Increased or unwanted hair growth • Increased risk of relapse • Thrombotic thrombocytopenic purpura (disorder that can lead to easy or excessive bruising and bleeding) • Electrolyte imbalances • Gingival hyperplasia (overgrowth of gum tissue around the teeth) • Increased risk of infection	• Pain in the hands and/or feet when administered intravenously. • Nausea • Vomiting • Liver problems • Kidney damage • Increases in cholesterol and triglyceride • Confusion	• Seizures • Vision changes • Dizziness

7. Mycophenolate Mofetil (MMF):

Likely (Over 10%)	Less Likely (1-10%)	Rare (Less than 1%)
• Nausea (feeling sick to stomach) • Miscarriage or birth defects if become pregnant while taking and within 6 weeks after stopping MMF • Headache • Insomnia • Electrolyte imbalances • Leg cramps/bone pain • Hypertension • Dizziness • Hyperglycemia • Rash	• 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)

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

Risks of Transplant

The following side effects may occur as a result of transplant and are not specific to cord blood as a donor or dilanubicel. We do not know if the risk of these side effects is increased by the use of dilanubicel.

Graft-versus-host-disease (GVHD). GVHD is a complication of transplant that can occur when another person's immune cells (specifically their T cells) react against the cells in your body. This is a risk of any unrelated donor transplant, though studies have shown that it is lower in cord blood transplant than in transplant with other donor types. It is possible that the use of dilanubicel (which is not matched to your HLA type) may make this risk higher, though this has not happened in prior studies. We think that this is unlikely because T cells from the cord blood to be expanded are removed before we grow the cells in the lab, and no new T cells are made during the process.

GVHD ranges from a mild skin disorder to severe involvement of the skin and/or liver, and/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 of GVHD: acute (generally occurs early in the transplant process) and chronic (generally occurs later in the transplant course and is longer lasting).

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 (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 steroids and 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 drugs that suppress the immune system, or it could be very severe. It may also last for several years, requiring continued use of multiple immunosuppressive drugs.

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 sinusoidal obstruction syndrome of the liver (SOS) due to the chemotherapy and/or radiation. Patients who have SOS 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.

Other complications. There may be additional side effects or complications not previously described in the consent form, which could be mild, moderate, or severe, or could even result in death.

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 drugs to reduce the chance of those infections, but these drugs 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.

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

Risks of Cord Blood as a Donor Source

The following problems may occur as a result of the use of umbilical cord blood as a donor source. We do not know if the risk of these side effects is increased by the use of dilanubicel.

Slow bone marrow recovery (delayed engraftment). Blood counts, including red blood cells, white blood cells, and platelets, may be very slow to recover after cord blood transplant. 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, but could also be life threatening. However, there are risks associated with the transfusion of red blood cells and platelets. These risks include serious allergic reactions and infections, including hepatitis, cytomegalovirus (CMV), and human immunodeficiency virus (HIV). All blood products will be screened for these infections in order to reduce risk.

Graft Failure. The cord blood stem cells may fail to “take” or engraft. This is a risk with any type of donor, but is more common with cord blood. Past experience suggests that this occurs in about 10-20% of cord blood transplant patients overall. The risk of graft failure may be higher in this study with the use of a single cord blood unit. There is a chance that if you have graft failure your blood counts may not recover and you could die from this problem. Should the graft fail, you may be able to receive a second transplant with stem cells from another donor, including additional cord blood donors.

Cytomegalovirus Reactivation. We have learned that patients who have been exposed to a virus called cytomegalovirus (“CMV”) before 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 cord blood transplant patients are at higher risk for reactivation of CMV, you 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.

Genetic Disease Transmission. It is very rare, but genetic diseases (such as thalassemia, sickle cell anemia or Gaucher's disease) may be passed to you through the transplanted cord blood stem cells or dilanubicel. Each 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 cord blood donor has been asked about the development of medical problems or known genetic diseases within the family to further reduce the possibility of passage of a disease to you from the cord blood cells.

Incorrect Labeling of the Cord Blood Unit. Though rare, it is possible that incorrect labeling of a cord blood unit could occur. Confirmation of identity will occur on every unit either by the cord blood bank providing the cord blood unit or by our institution. Should the labeling be incorrect, the transplant will be delayed until another source of stem cells is located.

Toxicities with Cord Blood Infusion – The unmanipulated cord blood cells can cause immediate toxicities, including allergic reactions, when the cells are infused. Immediate toxicities can happen either during or within the first 24 hours following either the infusion of the expanded and unmanipulated cord blood cells. In addition, the unexpanded cord blood cells are stored in a solution containing dimethyl sulfoxide (DMSO) to protect the cells during freezing, and are thawed in a solution containing dextran. DMSO and dextran can cause the following side effects, including allergic reactions, when the cells are infused.

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

If immediate toxicities occur, the infusion of either of the cord blood stem cells will be stopped and side effects will be closely monitored. Infusion of the cells may be restarted at a slower rate when all side effects have gone away.

Risks of dilanubicel

Dilanubicel is an investigational therapy and not all risks are known. By being in this research study, you may be at greater risk than you would otherwise be.

Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. In some cases, side effects can last a long time or never go away. You should talk to your doctor about any side effects that you have while you are in this study.

Dilanubicel Infusion Reactions: Immediate infusion reactions are possible, and they may occur either during the dilanubicel infusion or within the first 24 hours following the dilanubicel infusion. These possible reactions could include:

- Fever
- Chills
- Fatigue
- Difficulty Breathing (Dyspnea)
- Rapid Breathing (Tachypnea)
- Chest Tightness
- Muscle Pain (Myalgia)
- Low Blood Pressure (Hypotension)
- Increased Heart Rate (Tachycardia)
- Low Oxygen in Your Blood (Hypoxemia)
- Reddening of the skin (Erythema)
- Hives (Urticaria)

Dilanubicel is frozen and stored in a solution containing dimethyl sulfoxide (DMSO) to protect the cells during freezing. DMSO can cause an allergic reaction and signs of an allergic reaction might include some of these above noted symptoms. You will be given medications (diphenhydramine and acetaminophen) to reduce the likelihood of an allergic reaction.

Some patients have experienced fever for unknown reason, which occurred more frequently in the first 1-3 days after infusion of dilanubicel. Although these fevers increased with higher dilanubicel doses, it is unknown why this happened and if it is related to dilanubicel, other treatment, or other reasons.

Some patients have experienced symptoms that resemble a severe infection or inflammatory syndrome occurring days to weeks after dilanubicel infusion. It is not yet known whether these symptoms are from an infection, due to the dilanubicel infusion or some other cause.

Alloimmunization: Alloimmunization is a condition in which your body makes antibodies (proteins) in response to proteins on the surface of infused cells that are not your own. In general, people don't have these antibodies unless they have had blood transfusions or were previously pregnant. Because dilanubicel is a cell therapy you could develop these antibodies. If you develop alloimmunization this could limit your ability to receive cells from certain donors if you need another bone marrow transplant.

Immediate Rejection of dilanubicel: Because dilanubicel is not matched to you or your cord blood donor, it is possible that there could be immediate immune-mediated rejection of dilanubicel. The cord blood stem cells may fail to "take" or engraft. As stated before, the risk of graft failure may be higher in this study with the use of a single cord blood unit. There is a chance that if you have graft failure your blood counts may not recover, which could be fatal.

Should the graft fail, you may be able to receive a second transplant with stem cells from another donor, including additional cord blood donors.

Transmissible Spongiform Encephalopathy: This product may carry a risk of transmitting diseases, such as Creutzfeldt-Jakob disease (CJD).

Incidental Findings: It is possible that the study procedures could find a possible medical problem that is unrelated to this study and that was previously not known to you. If the research procedures uncover findings that may be important for you to know about, such as the possibility of a previously not known medical condition, you will be told by a member of the study staff. Or, you may allow the release and communication of the findings to your primary physician. These findings may require more testing or treatment. The cost of any additional tests or related treatment will be your responsibility.

Reproductive Risks

Chemotherapy and radiation treatments may make you sterile (unable to have children). The effects of dilanubicel on pregnancy, an unborn baby, or a nursing child are not known. Also, the drugs in this study may affect a baby, before or after the baby is born.

*For women who can become pregnan*t:

- You should not become pregnant while you are in this study.
- You should not nurse a baby while you are in this study.

For women and men:

- If you are having sex that could lead to pregnancy, you should use birth control while receiving study treatment and for at least 90 days after transplant and dilanubicel infusion.
- Check with the study doctor about birth control methods and how long to use them. Some common methods might not be appropriate while you are in this study.

What are the benefits?

We do not know if this study would help you.
Patients who get treatment in this study may get better, but their condition could stay the same or even get worse. We hope the information from this study will help other people with HIV and leukemia and lymphoma in the future.

You have other choices besides this study.

You do not have to join this study. You are free to say yes or no. Your regular medical care will not change. If you do not join this study, you have other choices for treatment.

Please talk to your doctor about your choices, which include:

- You may be eligible for a single unit or double unit cord blood transplant without the use of dilanubicel;
- Ongoing conventional chemotherapy may also be considered as an alternative to transplant in treatment of your cancer;
- No further treatment; and
- Comfort care.

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;
- Fred Hutchinson Cancer Center (Fred Hutch), and University of Washington (UW);
- US National Institutes of Health, National Cancer Institute, Office for Human Research Protections, Food and Drug Administration, and other agencies as required;
- Center for International Blood and Marrow Transplant Research (CIBMTR);
- Cord Blood Bank (that provided the unmanipulated unit or units for your transplant);
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Center IRB. An IRB is a group that reviews the study to protect your rights as a research participant.
- Deverra Therapeutics and their agents. Deverra is a company that is collaborating with Fred Hutch on this study.

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

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

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

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 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 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.

How is my genetic information protected?

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

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

- Asking for genetic information obtained in research studies, or
- Using genetic information when making decisions regarding your eligibility or premiums

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

Would we pay you if you join this study?

There is no payment for being in this study.

Would you have extra costs if you join this study?

If you join this study, you would have some extra costs. Your insurance company might pay these costs, but some insurance policies do not cover these costs. We could help find out whether your insurance company would cover these costs.

The extra costs are:

- Cost of tests that are given more often than usual.
- Paying the people who give dilanubicel, and the cost of the equipment they use.
- Cost of standard doctor visits and lab tests.
- Cost of any other medical care needed because of this study.

If you join this study, you or your insurance company would have to pay for the costs of standard treatment in this study.

You would **not** be billed for:

- The cost of the dilanubicel
- The cost of the research tests that are not part of your clinical care and tests to study how your immune system is recovering.

If dilanubicel is approved as a treatment while this study is still going on, you or your insurance company might have to pay for dilanubicel in order to complete this study.

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

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

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

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

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

What will my information and blood and tissue samples be used for?

Your information and blood and tissue samples will be used for the purposes of this study.

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

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

In addition, be aware that by agreeing to participate in this study, your information or tissue samples could be used for future research studies or sent to other investigators for future research studies without additional consent from you. These future research studies will be reviewed by an oversight group known as an institutional review board if required by law. The information that identifies you will first be removed from your information or tissue samples. If you do not want your information or tissue samples to be used for future research studies without your consent, you should not participate in this study.

Your tissue contains DNA. DNA makes up the genes that serve as the "instruction book" for the cells in our bodies. By studying genes, researchers can learn more about diseases such as cancer. There are many different types of genetic tests. The testing on your tissue samples might include genetic testing called whole genome sequencing. Whole genome sequencing looks at all the known genes in your cells. This type of testing can provide useful information to researchers. It can also present risks if the test results became known to others, for example you could have problems with family members or insurance companies. There is also a risk that these test results could be combined with other genetic information to identify you.

We invite you to donate left over tissue samples for research.

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

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

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

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

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

If you donate tissue for research, you could withdraw the donation at any time by calling Dr. Filippo Milano at (206) 667-5925. You would have no penalty for withdrawing the donation, and regular medical care would not change. We could not return donated tissue, but we might be able to destroy the donated tissue. We could not destroy tissue if it is stored or shared without any label saying who donated it. In this case, it could still be used for research.

Future genetic research

Several genetic databases are available to help researchers understand different diseases. These databases contain DNA code and medical information from participants who have various diseases.

As part of this study, we would like to release DNA code and information about your medical condition into a genetic database in order to help future research. The genetic database would not contain names, addresses, or other information that could be used to identify you.

The DNA code in a genetic database cannot be used by itself to identify any specific person. A researcher who already has DNA code about you could use information from a genetic database to learn more about you. Once we release information to a genetic database, we no longer have any control over the use of this information.

Patient Responsibilities

If you join this research study, you will have the following responsibilities:

- Go to all scheduled visits.
- Tell your study doctor before taking any new medications.
- Follow the study staff's directions about the study.
- Tell the study doctor about any illnesses or injuries.
- Tell the study doctor about any side effects or problems that occur during the study.
- Tell the study doctor if you plan to have any surgery or any other medical treatment or procedure.

During the study, you will not be allowed to take certain medications. This means some prescription medications. It also means certain over-the-counter supplements and herbal medications. The study staff will let you know which medications you cannot take during the study.

Your rights

- You do not have to join this study. You are free to say “yes” or “no”.
- If you get sick or hurt in this study, you do not lose any of your legal rights to seek payment by signing this form
- During the study, we might learn new information that you need to know. For example, some information may affect your health or well-being. Other information might make you change your mind about being in this study. If we learn these kinds of information, we would tell you.
- If you join this study, you would not have to stay in it. You could stop at any time (even before you start). Your regular medical care would not change. You would have no penalty for stopping, but it would be better not to join the study if you think that you would change your mind later.
- If you decide to drop out, we would want you to tell the study doctor. The doctor could tell you about the effects of stopping dilanubicel and/or study treatments described beneath the section titled *Conditioning (Pre-transplant Chemotherapy and Radiation)*. You and the doctor could talk about the follow-up care and testing that would help the most.
- Before you leave the study, the doctor might ask you to sign a separate consent form to continue in the follow-up part of the study.

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

For more information

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

If you have questions about:	**Call:**
This study (including complaints and requests for information)	206-667-5925 (Dr. Filippo Milano)
If you get sick or hurt in this study	206-667-5925 (Dr. Filippo Milano)
Your rights as a research participant	206-667-5900 or email irodirector@fredhutch.org (Director of Institutional Review Office, Fred Hutchinson Cancer Center)
Your bills and health insurance coverage	206-606-1113

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

Read the following question and think about your choice. When you decide on the question, please circle **YES** or **NO**.

Is it OK if we send your genetic information to one or more databases for future research? (circle one) **YES** **NO** Do you agree to donate your leftover samples (either fluid or tissue samples) for research? (circle one) **YES** **NO**

Signatures

Please sign below if you:

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

Participant (age 14+):

Printed Name	Signature	Date

Parent or legal guardian:

Printed Name	Signature	Date

Legally Authorized Representative: Please sign below if you:

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

Legally authorized representative:

Printed Name	Signature	Date

Relation to the participant

If you served as an interpreter or 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	Date

Researcher's statement

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

Person obtaining consent signature:

Printed Name	Signature	Date

Protocol RG1004070
Current version date: September 2, 2022
Previous version date: May 25, 2021
Copies to Study Participant, Medical Records, Research File