

**CAROLINAS HEALTHCARE SYSTEM  
CONSENT TO PARTICIPATE IN A RESEARCH STUDY**

**A Phase II Study Using the CliniMACS® Device for CD34<sup>+</sup> Cell Selection and T Cell  
Depletion for Graft-versus-Host Disease Prophylaxis in Alternative Donor Stem Cell  
Transplant Recipients**

**Adult Recipient (receive) and Parent of Minor Recipients**

When we say “you” in this consent form, we mean you or your child; “we” means the doctors and other staff.

**INTRODUCTION**

Dr. Andrew Gilman and his associates are asking you to participate in this research study at Levine Children’s Hospital (LCH)/Carolinas Medical Center (CMC)/Carolinas HealthCare System (CHS).

Details about this study are discussed below. You are being told this information so that you can decide in a free and informed manner whether you want to participate. You will be given a copy of this consent form. You are urged to ask your study doctor, or staff members who may assist them, any questions you have about this study at any time.

You are being asked to participate because you are being considered for a bone marrow (soft tissue inside the bones) stem cell transplant. A histocompatible (tissue matched) donor (person giving the stem cells or bone marrow) who is related to you is preferable but is not available. It is for this reason that you are being asked to participate in this study. An alternative donor (matched unrelated donor or half-matched [haplocompatible] related donor) is available to donate for you.

Bone marrow transplantation (BMT) is used as part of treatment for certain cancers, inherited diseases and marrow failure syndromes. One source of bone marrow stem cells is the blood, which circulates throughout the body in arteries and veins. In addition to red cells (carry oxygen from the lungs), white cells (fight infections) and platelets (stop bleeding), blood contains small numbers of bone marrow stem cells called peripheral blood stem cells (PBSC). These cells can be collected along with other white blood cells by a process called leukapheresis. Bone marrow or PBSC from a healthy donor can be transplanted (given) into a recipient in order to restore the

bone marrow following high dose chemotherapy and radiation therapy—which are used to kill cancer cells and bone marrow cells and to prevent rejection of the donor cells.

A major problem after a transplant from an alternative donor (donor other than a matched related donor) is Graft-versus-Host Disease (GVHD). GVHD occurs when donor T cells that are passed to the recipient with the donor PBSC attack certain tissues or organs (for example, the skin, liver, intestines) of the transplant recipient. A T cell is one type of white blood cell that is important for fighting infection and cancer cells in the body. The risk of GVHD is increased when the donor is mismatched with or unrelated to the recipient.

Methods are now available for selecting stem cells and removing T cells from PBSC. One **investigational** technique that is being evaluated uses the CliniMACS® CD34<sup>+</sup> Reagent System from Miltenyi Biotec, Inc. This involves capturing the stem cells in the PBSC with a monoclonal antibody (protein that recognizes a target) attached to a special iron chemical. When placed in a powerful magnetic field, the antibody-bound stem cells are selected and the T cells are washed away, that is, depleted. The device that is used is investigational, which means that it has not been approved by the U.S. Food and Drug Administration (FDA) for this indication. Over 500 transplants have been done using the CliniMACS® device to select stem cells and remove T cells. Based on the results, it appears that enough T cells can be removed to significantly reduce the risk of GVHD. The CliniMACS® CD34<sup>+</sup> Reagent System from Miltenyi Biotec, Inc. was approved by the FDA in January, 2014 as a Humanitarian Use Device for the processing of PBSC to obtain a CD34-enriched stem cell collection for adults with acute myeloid leukemia in first complete remission undergoing PBSC transplant from a matched related donor without the needs for medications to prevent GVHD.

The purpose of this research study is to determine the ability of stem cell selection and T cell depletion using the CliniMACS® device to prevent severe graft-versus-host disease after a stem cell transplant from an alternative donor.

Approximately 30 patients with a matched unrelated donor and 60 patients with a half-matched [haplocompatible] related donor will take part in this study at LCH/CMC.

### **HOW THE STUDY WORKS**

During the course of this study, the following will occur:

1. You will have several blood tests (requiring approximately 20 ml [4 teaspoons] of blood) to check kidney and liver function as well as past exposure to certain viruses including cytomegalovirus (CMV), hepatitis, and human immunodeficiency virus (HIV). In addition, you will have pulmonary (lungs) function tests and an electrocardiogram (EKG) and echocardiogram (to check the heart). You will also have a dental (teeth) exam. Some of these tests may be done locally by your referring doctor or at CMC/LCH.

As part of this study, you will be tested for HIV. You will be notified of the results of this testing and counseled as to the meaning of the results, whether they are positive or negative. If the test indicates that you are infected with HIV, you will receive additional counseling about the significance of your care and possible risks to other people. We are required to report all positive results to the North Carolina State Board of Health. The test results will be kept confidential to the extent permissible under the law. If you do not want to be tested for HIV, then you should not agree to participate in this study.

2. Approximately 2 ounces of blood will be drawn from you, your parents, and your brothers and sisters to determine tissue types. This typing will help choose the best donor for you.

3. If you don't already have one, a central intravenous (through a vein, IV) catheter (small tube) that contains two lumens (openings) will be inserted into a large vein in your chest under sedation or general anesthesia. This catheter is essential for giving drugs, blood products and fluids, drawing blood and providing nutritional support.

4. The donor peripheral blood stem cells (PBSC) will be collected from your donor and will be shipped to a Stem Cell Processing laboratory at the University of California-San Francisco to be processed using the CliniMACS® device. After processing, the PBSC will be frozen. The PBSC will be shipped to Levine Children's Hospital when needed. The PBSC will be thawed and infused (given) into you on Day 0 of transplant.

5. Following admission to the BMT unit at LCH, you will receive a patient-specific conditioning regimen that may include total body irradiation (TBI), fludarabine, thiotepa, rabbit anti-thymocyte globulin (Thymoglobulin®, rATG), melphalan, busulfan, cyclophosphamide, and/or rituximab. These drugs and TBI are given to kill any cancer cells, destroy your own bone marrow cells and to prevent rejection of the donor stem cells. If your conditioning regimen includes TBI, you will meet with the Radiation Therapy specialists to discuss this procedure in detail and they will answer any questions you have. Patients who do not receive TBI and have a

history of Epstein-Barr virus (EBV) infection will receive a dose of Rituximab on Day -1 to try to prevent complications due to EBV (see below in RISKS section).

- a. The standard regimen will be Total Body Irradiation (TBI) followed by chemotherapy. The schedule of therapy is as follows:

Day -9 TBI  
Day -8 TBI  
Day -7 TBI  
Day -6 Thiotepa and fludarabine  
Day -5 Fludarabine and rabbit ATG  
Day -4 Fludarabine and rabbit ATG  
Day -3 Fludarabine and rabbit ATG  
Day -2 Fludarabine and rabbit ATG  
Day -1 Rest  
Day 0 Transplant

The day listed above is the day prior to the stem cell transplant. For example, Day -9 refers to 9 days before the transplant.

- b. For patients who have a contraindication to TBI or a non-malignant disease, a Chemotherapy Alone Regimen may be used. The schedule of therapy is:

Day -7 Melphalan  
Day -6 Thiotepa and fludarabine  
Day -5 Fludarabine and rabbit ATG  
Day -4 Fludarabine and rabbit ATG  
Day -3 Fludarabine and rabbit ATG  
Day -2 Fludarabine and rabbit ATG  
Day -1 Rituximab (if indicated)  
Day 0 Transplant

- c. Depending on your disease, the conditioning therapy may be modified to include other chemotherapy drugs (melphalan, busulfan, and/or cyclophosphamide), with or

without TBI. If you require an alternate conditioning therapy, you will have the following schedule for your therapy (the drugs given will depend on your disease):

Day -9 \_\_\_\_\_  
Day -8 \_\_\_\_\_  
Day -7 \_\_\_\_\_  
Day -6 \_\_\_\_\_  
Day -5 \_\_\_\_\_  
Day -4 \_\_\_\_\_  
Day -3 \_\_\_\_\_  
Day -2 \_\_\_\_\_  
Day -1 \_\_\_\_\_  
Day 0 Transplant

6. It usually takes 2-3 weeks for the donor cells to grow and begin producing enough red cells, white cells and platelets. During that time you will be in protective isolation (steps will be taken to prevent exposure to infection) in your blood and marrow transplantation (BMT) room. Once your neutrophil (a white blood cell that fights infections) count is greater than 500, your transfusion requirements are no more than every other day, and there is no evidence of infection, you will be discharged from the hospital. Depending on how far from LCH you live, you may need to stay locally for the first 100 days after transplant. The average hospital stay for a recipient of this type of transplant is 4-5 weeks.

7. You will be given the option to participate in a companion study to help your immune system recover more quickly if you meet the study eligibility criteria after transplant. You will sign a separate consent for this companion study.

8. Following discharge, you will be seen in the BMT Clinic at LCH at least weekly until 100 days after transplant, at least monthly until 1 year after transplant (but sometimes still weekly to every other week), every three months for the next year, every 6 months for the following year and yearly thereafter until 5 years post transplant. At those visits, blood (2-4 tsp) may be taken to monitor engraftment (presence of donor cells) and recovery of your immune system (ability to fight infection). You will also have routine BMT follow-up including blood tests to check the function of your kidneys and liver and yearly evaluation of the lungs (pulmonary function testing) and heart (ECG and echocardiogram).

### **Length of Study**

Your participation in this study will include a hospital stay of approximately 4-5 weeks. Following discharge, you will be seen in the BMT Clinic until 5 years after transplant.

### **RISKS**

This study has several risks. Many of these risks are seen with any type of stem cell transplant. The use of T cell-depleted PBSC may be associated with a higher risk of infection and lower risk of GVHD than some other types of alternative donor transplants. In addition to the known risks listed below, there may be uncommon or unknown risks that might occur.

### **Short term effects of chemotherapy and radiation**

Many side effects are common to the high-doses of chemotherapy drugs used for transplant. These include:

#### **Likely:**

- Anemia (decrease in red blood cells) and a severe decrease in white cells and platelets. You will require intensive treatment for these problems including frequent transfusions of red cells and platelets, as well as antibiotics (drugs) for infections.
- Hair loss
- Nausea
- Vomiting
- Loss of appetite
- Mouth sores
- Diarrhea

#### **Less Likely:**

- Bleeding and/or infections that can be fatal (causing death).
- Damage to the lungs, liver, and/or kidneys. This may result in mild temporary decreased function of these organs, chronic (long term) decreased function that may limit your normal activities, or progressive severe deterioration (worsening) and death.

#### **Rare but Serious:**

- Damage to the heart and/or brain. This may result in mild temporary decreased function of these organs, chronic dysfunction that may limit your normal activities, or progressive severe deterioration and death.

### **Long-term effects of chemotherapy and radiation**

#### **Likely:**

- Sterility (inability to have children)
- Effects on growth

#### **Less Likely:**

- 10-20% likelihood of cataracts (clouding of the lens in the eye)
- Decreased thyroid function (thyroid gland makes less thyroid hormone)

#### **Rare but Serious:**

- Slowed mental development
- There is an increased risk (1-15%) of another cancer (leukemia, lymphoma, skin cancer) in the future. Leukemia or lymphoma may occur as a result of the transplant. Skin cancers may also occur as a result of the transplant, especially if total body irradiation is used. The risk for this is approximately 1 in 100 for every ten years you live after the transplant.

### **Specific side effects and complications for each drug and radiation not listed above include:** **Total Body Irradiation (TBI)**

#### **Likely:**

- Dryness of the skin.

#### **Less Likely:**

- Dryness of the mouth, sore throat and/or thickened saliva (spit)
- Swelling (like mumps) of the saliva glands in the cheeks
- Fever
- Sunburn appearance of the skin starting several days after radiation therapy

#### **Rare but Serious:**

- Damage to the brain
- Irritation of the lungs (pneumonitis) and the sack surrounding the heart (pericarditis).

### **Fludarabine**

#### **Likely:**

- Increased risk of infection from viruses and other germs

**Less Likely:**

- Inflammation of the liver

**Rare but Serious:**

- Damage to the nerves causing tingling or pain and/or weakness
- At higher doses than used in this study, has been associated with brain damage, causing blindness, confusion and coma (unconsciousness)
- Disorders of the immune system causing damage to red cell or platelets

**Thiotepa**

**Likely:**

- The skin will darken after getting thiotepa and this can take months to return to normal. A skin rash and breakdown of the skin may occur in areas where the skin rubs together, that is, the neck, arm pits and in the groin. These may be painful and can become infected. With preventive measures, these are usually prevented.

**Less Likely:**

- Damage to the liver and lungs

**Rare but Serious:**

- Sleepiness, forgetfulness, confusion, hallucinations (seeing things that aren't there), and seizures (usually just in patients that have had radiation to the brain before transplant)

**Rabbit anti-thymocyte globulin, rATG, Thymoglobulin®**

**Likely:**

- Fevers and shaking chills during or soon after it is given and, in 25% of patients, an allergic type rash. These signs and symptoms go away after the rATG has been given.
- Delay in immune system recovery (ability to fight infections)

**Rare but Serious:**

- There is a slight (less than 1%) chance of a severe allergic reaction (anaphylaxis) to rATG that could result in severe symptoms involving difficulty breathing and heart failure. Usually, these symptoms can be treated, and they go away with stopping the drug, but, in their most severe form, these reactions can be fatal.



### **Melphalan**

#### **Less Likely:**

- Irritation of the lung
- Inflammation of the liver

#### **Rare:**

- Damage/scarring of lung or liver tissue

### **Busulfan**

#### **Likely:**

- Temporary darkening of the skin

#### **Less Likely:**

- Liver damage

#### **Rare but Serious:**

- Lung scarring
- Seizures (rare because medicine to prevent seizures is given with the busulfan).

### **Cyclophosphamide**

#### **Less Likely:**

- Water retention
- Hiccups
- Nasal congestion, runny nose, sneezing
- Liver damage

#### **Rare but Serious:**

- Damage to the lining of the bladder leading to blood in the urine (rare when a drug to protect the bladder is given with the cyclophosphamide)
- Damage to the lungs and heart
- Irregular heart beat

## **Rituximab**

### **Less Likely:**

- Fever
- Chills
- Nausea
- Weakness
- Headache
- Low blood pressure
- Itching
- Rash
- Bronchospasm (an abnormal narrowing of the windpipe which can be associated with coughing and wheezing)
- Abdominal pain
- Vomiting
- Anemia
- Achy joints and muscles
- Dizziness
- Congestion
- Low blood counts.
- Suppression of certain parts of your immune system resulting in a greater risk of infections

### **Rare but Serious:**

- Angioedema (a condition characterized by an itchy rash and swelling of areas of the skin and mucous membranes [the lining of some of the organs], much like an allergic reaction)
- Severe reactivation of hepatitis B infection and liver failure
- Progressive multifocal encephalopathy (Most people, as children, have been infected with a virus called JC virus. In most cases this virus does not cause any problems, but in very rare cases of patients who receive rituximab, this virus can become active again, leading to severe damage to the brain tissue.)

### **Methylprednisolone**

#### **Less Likely:**

- High blood pressure
- High blood sugar
- Increased risk of infection

#### **Rare:**

- High or low heart rate

### **Risks of Transplantation**

The chance of a child dying from a T cell-depleted transplant-related complication is approximately 10-30%. This is similar to the risk with an unrelated donor transplant (bone marrow, PBSC, or cord blood) that has not been T cell-depleted. The chance of dying depends upon a number of factors including the transplant patient's past history, the disease for which the transplant is being performed, and the patient's state of health at the time of transplant. Risks that are more or less common with T cell-depleted transplants are:

#### **Likely:**

- 1. Cytomegalovirus (CMV) infection:** A relatively common complication in BMT patients is CMV infection. CMV is a common infection in the first several years of life. About half of all people have been infected and CMV remains in a quiet state in the body. CMV can be also be passed in blood and bone marrow infusions. The chance of passing CMV is decreased by the CD34<sup>+</sup> selection process. During the transplant period, CMV that is already in the body can become reactivated (referred to as infection) and result in disease of the lungs (pneumonia), eyes, brain, liver, and/or intestines. In recipients of T cell depleted transplants who have previously been infected, the risk of having CMV reactivation (having the infection again) is 50-60%. You will be given anti-viral drugs that may include ganciclovir, foscarnet, and acyclovir to try to prevent CMV reactivation. Ganciclovir, and less commonly acyclovir, can suppress bone marrow growth and damage the kidneys. Foscarnet can also damage the kidneys but usually doesn't affect blood counts. Your blood counts and blood tests of kidney function will be watched for these side effects. Also, frequent blood tests will be done to look for CMV reactivation. If there is evidence of reactivation, additional treatment will be given to you. Ganciclovir and/or foscarnet will be given. If CMV reactivation progresses to disease, it may be fatal.

2. **Adenovirus infection:** A relatively common complication in BMT patients is adenovirus infection. Adenovirus is a common infection in people in general that causes a cold or stomach flu. During the transplant period, adenovirus that is already in the body can become reactivated (referred to as infection) and result in disease of the lungs (pneumonia), liver, and/or intestines (vomiting, diarrhea). The risk of having adenovirus reactivation (having the infection again) is 50%. Frequent blood tests will be done to look for adenovirus reactivation. You will be given an anti-viral drug named cidofovir if adenovirus reactivation occurs. This usually prevents adenovirus disease. If adenovirus reactivation progresses to disease, it may be fatal. Cidofovir can suppress bone marrow growth and damage the kidneys. Your blood counts and blood tests of kidney function will be watched for these side effects and the cidofovir dose will be adjusted if necessary.
3. **Prolonged immunodeficiency:** Under normal circumstances, when using a matched related donor it usually takes about 3 months for the immune system to start functioning. With a CD34<sup>+</sup> selected, T-cell depleted PBSC transplant, this may be delayed to 6-12 months. During the time that you are unable to fight infection, there will be an increased risk of infections that could be fatal. You will likely receive gammaglobulin (antibodies purified from donor blood that help to protect the body against bacterial and viral infections) infusion after transplant. It will be given to decrease the risk of infection until your immune system can make antibodies. It is possible that you will require monthly infusions of gammaglobulin for a long time after transplant (more than 6 months to 1 year). There is a small chance that you could require IV gammaglobulin for the rest of your life.

**Less Likely:**

1. **Graft failure:** There is a chance that the donor PBSC will not grow after transplant or will be rejected by your immune system. The graft failure or rejection rate is approximately 10% but could be as high as 20%. If graft failure occurs, it is possible that there will be not be enough platelets, white blood cells and red blood cells to prevent bleeding and infection and if uncorrected this could be fatal. If graft failure occurs, then re-transplantation using the same or another donor would be necessary for survival, which would require further giving of chemotherapy.
2. **Graft versus Host Disease (GVHD):** Graft-versus-host disease (GVHD) is a reaction in which the donor T cells attack the recipient's body. It ranges from a mild skin disorder to severe involvement of skin, liver, and/or gut and it may be fatal for some patients. Many

(20-60%) transplant recipients who receive bone marrow or PBSC that have not had T cell removed experience acute and/or chronic GVHD. About 20-25% of patients will have severe GVHD, which can be fatal. The removal of T cells used in this study significantly reduces the chances of developing GVHD. The chance of acute and chronic GVHD occurring is about 20-25% for each. There is a small chance (less than 5%) of severe, possibly fatal, GVHD. Signs of GVHD include:

A. Acute GVHD generally occurs within 1 - 4 weeks of receiving donor T cells, but it may occur after a longer period of time. Acute GVHD can lead to:

- Skin damage – sunburn-like rash, peeling, burn
- Intestinal damage – diarrhea, nausea, vomiting, stomach pain, bleeding
- Liver damage – yellow skin, decreased liver function

Severe acute GVHD can also uncommonly affect the lungs.

B. Chronic GVHD usually occurs more than 100 days after receiving donor T cells, but may occur earlier. Chronic GVHD can be life-threatening. It can also result in you not feeling well and being able to do normal activities, sometimes for a long time. Chronic GVHD can affect many parts of the body. The most commonly affected areas are the skin, mouth, liver, and eyes. Chronic GVHD can cause:

- Skin rash, skin thickening, dark color of skin, loss of color of the skin, loss of hair, thin hair, and gray hair
- Dry mouth and eyes, mouth sores
- Joint pain and stiffening, inability to move joints
- Nausea, vomiting, diarrhea, abdominal cramps, weight loss, decreased appetite, inability to absorb medications or food, difficulty swallowing
- Liver inflammation
- Lung damage, cough, shortness of breath, wheezing
- Breakdown of red blood cells and platelets

3. **HHV-6 infection:** Human Herpes Virus 6 (HHV-6) is a common infection in the first several years of life. Like CMV, it remains in a quiet state in the body. During the transplant period, HHV-6 can become reactivated and cause GVHD or graft rejection. To prevent this, you will be given an anti-viral drug called foscarnet from the time of transplant until discharge. Foscarnet can decrease kidney function and cause loss of salts from your blood. These effects are usually temporary and go away when the drug is stopped.

- 4. Epstein-Barr virus (EBV) infection:** EBV is a common infection in the first several years of life. About half of all people have been infected and EBV remains in a quiet state in the body. When the immune system is very weak, EBV can reactivate and cause B cells (a type of white blood cell) to multiply. This process, known as post-transplant lymphoproliferative disease (PTLD), can cause fevers, swollen lymph nodes (organ that has white blood cells) and tonsils (part of the lymph system), and difficulty breathing. It can also become lymphoma, or a cancer of lymph nodes. If treated early, patients often do well. However, PTLD can progress and be fatal. We will monitor your blood for EBV reactivation and treat you for reactivation or early PTLD. The treatment is typically a drug called Rituximab. Rituximab can cause fever and chills. It will also slow the ability of your immune system to make antibodies.
- 5. Relapse of leukemia:** In patients with leukemia who receive a matched related donor transplant, the chances of leukemia recurring (returning) after transplant varies from 10-50% depending upon the type and stage of leukemia. With T-cell depleted transplants, the relapse (cancer coming back) rate may be higher, especially for patients who lack certain immune system mismatches with the donor.
- 6. Inadequate number of donor PBSC:** There is a chance that not enough PBSC will be collected from your donor. The chance of not having enough PBSC is very small if a mismatched related donor is used. If this happens, PBSC will be collected from another donor. If an unrelated donor is going to be used, your transplant doctor will decide if you can receive the transplant without removing the T cells if not enough PBSC are collected to remove the T cells. If this is the case, you will get PBSC with the T cells that were collected if not enough PBSC are collected. If your transplant doctor decides that the T cells must be removed, then you will only be eligible to be on study if your weight is:

  - 37 kg (about 81 lbs) if your donor's PBSC are collected in 1 day
  - 26 kg (about 57 lbs) if your donor's PBSC are collected in 2 days

The difference in weight is because more PBSC are collected with a 1 day collection. The choice of 1 or 2 days of collection is up to the donor and PBSC collection center. We will always request a 1 day collection. If not enough PBSC are collected and you need to have the T cell removed, then PBSC will be collected from another donor.
- 7. Thrombotic microangiopathy (TMA):** Uncommonly, patients may develop very small blood clots. The clots usually occur in the kidneys but might occur elsewhere. TMA can occur in any type of transplant. TMA usually occurs in patients with viral or fungal

infections and therefore may be more common when T cells are removed. TMA can result in decreased kidney function, high blood pressure, and lower red blood cell and platelet counts. There are treatments for this problem but it can be life-threatening.

**Rare but Serious:**

- 1. Contamination of stem cells:** It is possible that an infection might be introduced into your body by the infusion of the processed stem cells. The stem cells will be tested before giving them to you in order to greatly lessen the chance of this happening.
- 2. Reaction to the chemicals in the stem cell infusion:** There is a risk of a reaction to small amounts of the antibody-iron dextran chemical that remains in the preparation of stem cells that is injected into you. Antibodies made in mice have been used to treat cancer and organ rejection for many years. While these typically cause flu-like symptoms, the amount of antibody that will be infused into you is less than 1% (1/100) of that used for cancer treatment. The iron dextran mixture is also used to treat anemia in much higher doses (1000 times higher) than the dose you will receive with the stem cell infusion. For these reasons it is believed that the likelihood of a reaction is extremely small (less than 1%).

**Complications seen with all types of transplants**

**Rare but Serious:**

- 1. Transfusion complications:** All blood products (platelets and red blood cell transfusions and gammagobulin) are handled as carefully as possible and are screened for compatibility with you as well as for infection with the hepatitis viruses and HIV, the virus that causes AIDS. However, there remains a very small chance that a reaction could occur or that infection(s) could be passed on to you.
- 2. Anesthesia (being put to sleep for surgery)**  
The risk of anesthesia for the placement of a central line (catheter) includes an unforeseen reaction to a medication that may be minor or result in death. The risk of dying from anesthesia in a healthy individual is less than 1 in 20,000. Minor symptoms following anesthesia include sore throat, nausea and vomiting.

**Reproductive Risks**

The treatment on this study can affect an unborn child. You should not become pregnant or breastfeed your baby while being treated on this study. If you are sexually active and are able to become pregnant or father a child, you and your partner must use birth control or you must not have sex. The study doctor will talk to you about good methods to avoid pregnancy while you are being treated on this study. Your doctor will talk to you about the length of time you need to avoid pregnancy or not have sex. If you have questions about this, please ask your doctor. If you or your partner becomes pregnant during the research study, please tell the study doctor and your doctor immediately.

### **RESEARCH TESTING (OPTIONAL)**

There will be additional optional research tests as part of this study. You can choose to participate in them but it is okay if you don't. In addition to the standard tests of recovery of the immune system, specialized research testing will be performed to gain more information about the quality of the immune recovery after transplant. These blood tests include:

- T cell receptor excision circle (TREC) analysis: this allows us to find out if new T cells are being made in your body
- V beta analysis: this allows us to see if there are just a limited number of T cells in your body or if the normal variety seen in people who have not had a transplant is present
- Flow cytometry for T and B cell subsets: this allows us to see which types of T and B cells are present and if they are maturing normally
- Flow cytometry for T cell activation: this allows us to see how T cells are responding
- CMV and EBV specific T cell analysis: this allows us to see if T cells capable of responding to these viruses are present in your blood.

The amount of blood taken at each time point will depend on your weight. The amount will be 2 mL/kg of body weight. For example, if you weigh:

- 10 kg (22 lbs): 20 mL (4 teaspoons)
- 20 kg (44 lbs): 40 mL (8 teaspoons)
- 30 kg (66 lbs) or more: 60 mL (12 teaspoons or 2 ounces)

\_\_\_\_\_ Yes, I consent to having research blood tests drawn at approximately 120 days, 6 months, and 1 year after my transplant. These tests will look at the recovery of my immune system.



\_\_\_\_\_  
No, I do not consent to having research blood tests drawn at approximately 120 days, 6 months, and 1 year after my transplant.

**EXCLUSION CRITERIA**

You should not participate in this study if you have an active infection or if you are pregnant.

**BENEFITS**

This study may or may not improve your condition. The information gained from your case may benefit others with your condition.

**ALTERNATIVE PROCEDURES/TREATMENTS**

You do not have to participate in this research study in order to receive treatment. Other procedures/treatments that are available include (1) unrelated donor transplant without T cell-depletion, (2) cord blood transplant, (3) not to have a transplant and receive chemotherapy and/or supportive care.

**ADDITIONAL COSTS**

You or your insurance carrier is responsible for payment of all procedures including hospital costs, laboratory tests including the collection and processing of the PBSC, and doctor's fees. Your insurance company may not pay for research treatments. You may wish to discuss coverage with your insurance company before agreeing to participate in this research study.

**COMPENSATION**

In the event that you are harmed as a result of your participation in this study, we will provide or arrange for treatment as necessary. This treatment, as well as other medical expenses, will be billed to you or your insurance company in the usual manner.

No other funds have been set aside to compensate you. However, by signing this form, you do not waive any of your legal rights.

You will not be paid for your participation in this study.

**WITHDRAWAL**

Your participation in this study is completely voluntary. You should feel under no pressure to be in the study. If you decide not to be in the study, it will not in any way harm your relations with your doctors or with Carolinas HealthCare System. You are free to stop being in the study if you

change your mind after entering it. This would not harm your relations with your doctors or Carolinas HealthCare System.

However, once intensive chemotherapy and total body irradiation is given to you, infusion of stem cells is absolutely necessary for survival since the drugs and total body irradiation will destroy the marrow cells in your body.

The investigators or sponsor also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, have failed to follow instructions, or because the entire study has been stopped.

We will tell you about new medical findings that may affect your willingness to continue in the study.

### **CONFIDENTIALITY**

The records of this study will be kept private. In any sort of report we might publish, we will not include any information that will make it possible to identify a patient. Your record for this study may, however, be reviewed and/or photocopied by Miltenyi Biotec, Inc., the manufacturer of the CliniMACS device, by Carolinas HealthCare System, or by representatives of the Food and Drug Administration or other government agencies. To that extent, confidentiality is not absolute.

Medical records are considered confidential and records are kept in a secured area accessible to those involved in your treatment. All data entered into a computer will be coded. No data that may be linked with you will be entered on any network computer allowing access to confidential information. The master list (linking your name to your health information) will be stored off-line and available only to the principal investigator and his or her designee(s). Although we will make every effort possible to maintain confidentiality, there is however, a slight risk of loss of confidentiality.

A description of this clinical trial will be available on [www.ClinicalTrials.gov](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.

### **AUTHORIZATION**

If you wish to take part in this clinical study, you will be asked to sign this consent form. It allows the study sponsor and the study investigator to collect, process and pass on to the sponsor organizations any relevant personal health information collected from you during the study. These are activities routinely carried out during all clinical studies.

You have been told that personal information about you (including sensitive personal health information, such as your medical history and your racial/ethnic origin if relevant to the study) will be reviewed, collected on a computer database, stored in electronic or manual files, audited, and/or otherwise processed by:

- the clinical study investigator, Dr. Gilman, and research staff,
- Miltenyl Biotech, Inc.,
- regulatory or other governmental authorities of the United States and other countries,
- other persons authorized by the study sponsor,
- Carolinas HealthCare System employees,
- other persons or agencies as required by law or allowed by federal regulations.

You have been told that your personal data are being collected and processed to:

- check your suitability to take part in the study,
- monitor your treatment,
- compare and pool treatment results with those of other subjects in clinical studies.

You have been told that your personal information may be processed within the U.S. or elsewhere in the world or transferred to or from the U.S. for review, processing and/or storage by an associated company or a carefully selected third-party organization. By signing this document, you explicitly consent to the transfer of your personal information, including sensitive personal information, collected during this clinical study, for review, processing and/or storage. Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the Privacy Rule. However, the groups are committed to keeping your personal health confidential.

You may refuse this authorization to transfer your personal information. If you choose not to agree to this authorization, you might be ineligible to participate in the study. If you decide not to sign this authorization, that will not harm your relations with your doctors or with Carolinas HealthCare System.

You have the right to inspect your medical record at any time. Your research record may be unavailable until the conclusion of the study. At that point, it will be available. Please speak with the study doctor if you desire to access your record.

You have been told whenever your personal information is processed; it will be kept confidential and secure, to the best of our ability. It will be used only for the purpose for which it was collected.

This authorization does not have an expiration date. You have been told that according to the guidelines for good clinical practice, the study investigator and sponsor will keep your personal information for at least 6 years. If you do not withdraw this authorization in writing, it will remain in effect indefinitely. If you wish to revoke authorization to use your personal information, you will notify the study doctor in writing at:

Andrew Gilman, MD  
Director, Pediatric Blood and Marrow Transplantation  
Levine Children's Hospital  
Carolinas Medical Center  
PO Box 32861  
Charlotte, NC 28232-2861  
Ph: (704) 381-6800

Some of the data obtained from your record prior to your revocation may still be used if considered necessary for the study.

#### **FINANCIAL INTERESTS OF THE INVESTIGATOR**

The doctors will receive no benefits in any form from the company that manufactures the investigational device being tested in this study.

#### **QUESTIONS**

The researchers doing the study at Carolinas HealthCare System are Dr. Gilman and his associates. You may ask them any questions you have now. If you have questions later, you may contact them at (704) 381-6800.

The Institutional Review Board is a group of people who review the research to protect your rights. If you have questions about the conduct of this study or about your rights as a research

subject, you may call the chairperson of the Institutional Review Board of Carolinas HealthCare System for information regarding patients' rights in a research study. You can obtain the name and number of this person by calling (704) 355-3158.

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**CONSENT**

I have read the above information. I have asked any questions I had, and those questions have been answered. I agree to be in this study and provide authorization for use of my personal health information. If a female of childbearing potential, I am not pregnant or breastfeeding. If I am able to become pregnant or father a child, I will use birth control. Dr. Gilman, one of his associates, or their designee will give me a copy of this form.

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<b>Patient (Representative*) Print Name</b>	<b>Date</b>	<b>Time</b>
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<b>Patient (Representative*) Signature</b>	<b>Date</b>	<b>Time</b>
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<b>Signature of Person Obtaining Consent</b>	<b>Date</b>	<b>Time</b>
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<b>Investigator Signature</b>	<b>Date</b>	<b>Time</b>
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\*Identity of representative:

\_\_\_\_ Next of Kin

\_\_\_\_ Parent/Guardian

\_\_\_\_ Healthcare Power of Attorney