*Affix Patient Label Here*



**Masonic Cancer Center, University of Minnesota**
**Blood and Marrow Transplantation Program**

# CONSENT TO PARTICIPATE IN RESEARCH

## Transplantation of Umbilical Cord Blood from Unrelated Donors in Patients with Hematological Diseases Using a Non-Myeloablative Preparative Regimen

**Investigator: Margaret MacMillan, MD, PhD**

You are invited to participate in a study because you have a cancer of the blood (a hematologic malignancy) and a stem cell transplant is recommended. This study is a continuation of research at the University of Minnesota using umbilical cord blood (UCB – cells collected at a baby's birth with permission from the mother and stored frozen in "bank" until needed by a patient) when a suitable donor is not available, and a less intensive (lower dose) chemotherapy/radiation combination before the transplant to prepare the body for the UCB cells.

Taking part in any clinical research involves risks and may provide some benefits. You need to understand these risks and benefits to make an informed decision about whether or not to be in this study.

This form is called a consent form. The intent of this form is to let you know the purpose of this study, the treatment plan, and the possible risks and benefits of participation. If you wish to take part in this study, you will be asked to sign this consent form.

Research studies only include people who want to take part. Please take time to make your decision. We encourage you to discuss your decision with your doctors, family, and friends.

This study is being conducted by the Masonic Cancer Center at the University of Minnesota Medical Center. The physician in charge of this study is Dr. Margaret MacMillan of the Blood and Marrow Transplantation (BMT) Program.

## Introduction

A stem cell (bone marrow) transplant consists of 3 major parts:

1) Administration of chemotherapy drugs and radiation therapy to clear space in the bone marrow for the donor cells. This is called the preparative or conditioning regimen;
2) Infusion of the thawed umbilical cord blood cells (the transplant) occurs shortly after the end of the preparative regimen; and
3) Post-transplant recovery period during which the donor cells take hold in the bone marrow (engraft) and begin to divide and grow into new blood cells as indicated by the recovery of the white blood cell, red blood cell and platelets recovering to normal levels.

Bone marrow transplants have been performed for over 40 years. Initially they used high doses of chemotherapy and radiation therapy to completely wipe out the patient's bone marrow cells and immune system before the donor cells (from either a relative or an unrelated donor) were given to "rescue" the patient. Over the years, it has been learned that using lower doses of chemotherapy and radiation therapy before the transplant is as effective with fewer side effects. The use of umbilical cord blood as an alternative source of donor cells has become common. In addition, new supportive care drugs or combinations have been tested improving transplant outcomes. As a result, transplant has become an option for older and/or patients with other medical issues.

In this study, a standard preparative regimen is used consisting of cyclophosphamide, fludarabine and a single dose of total body irradiation. Our previous study, which enrolled over 250 patients since 2005, evolved over time. Originally the dose of fludarabine was higher and the drugs to prevent acute Graft-vs-Host Disease (aGVHD – a common complication of transplant) were different. aGVHD occurs within the first few months after the transplant because the donor cells (UCB) see the patient's body as foreign triggering a response by the immune system. It commonly involves the skin, liver, and the intestines with symptoms such as a skin rash, jaundice (yellowing of the skin), nausea, vomiting and diarrhea. Drugs are routinely given after the transplant to suppress (hold down) the immune system to prevent or lessen the severity of the reaction. Suppressing the immune system has some bad effects including increasing the risk of infection. This current study follows the last treatment plan used in the previous study.

**Research Component Of This Study**

Our data comparing with this immune suppression regimen to the previous regimen resulted in similar engraftment, acute GVHD and non-relapse mortality. However, before we can definitively adopt this immune suppression regimen as our new standard of care, we need better define its safety and efficacy profile in larger numbers of patients. The goal of this study is to collect data on additional patients using the previous study's final treatment plan to confirm the findings of good transplant outcomes with a low rate of GVHD. It is felt that reducing the occurrence of GVHD after a transplant would quicken patient recovery lowering the risk of infections and disease recurrence. Information collected during this study (transplant outcomes and side effects) will be compared with the outcomes of our previous transplant study that enrolled more than 250 patients.

Up to 165 persons will be enrolled in this study over the next 6 to 10 years.

**Risk of Participation in this Research**

Albeit unlikely, the main risk related to the research component of this study is the disclosure of private health information to unauthorized individuals. Also, unlikely but possible is that as our experience with this regimen grows the result are not as good as we initially found. The study will be monitored twice yearly by the Masonic Cancer Center Data and Safety Monitoring Board.

**Standard Transplant Procedures**

The appendices attached to this consent form has detailed information on toxicity of specific drugs and the risks potential complications that every marrow, blood, and umbilical cord blood transplantation patient are exposed to.

**Pre-transplant evaluation:**

You will undergo routine tests and evaluations to find out if you are healthy enough to undergo a transplant, including:

- medical history and physical examination, including height and weight.
- routine blood tests (approximately 1-2 tablespoons) to assessorgan function and disease status.
- A pre-transplant viral panel (requiring 1 tablespoon of blood) to check for exposure to viruses, including hepatitis and HIV. If you test positive for hepatitis or HIV, you

will not be eligible to take part in this study. It will be recommended that a Blood Bank physician contact your personal physician regarding possible further testing. By law the Minnesota Department of Health must be notified if you test positive for hepatitis or HIV.

- If you are a woman able to have children, a pregnancy test will also be performed. If you are pregnant, you will not be able to take part in this study.

Additional tests may be done to evaluate your disease and general health.

If you do not already have one, a central line will be placed to allow easier administration of intravenous (IV) therapies. A central venous catheter is a flexible sterile tube that will be placed into a large vein that runs under your collarbone so that blood can be withdrawn and medications given more easily and with less discomfort. This tube usually is placed under local anesthesia (you are awake).

**A note about day counts:** The transplant (UCB cell infusion) is done on what is called day 0 (zero). Treatment given before day 0 is counted out in negative day numbers, i.e. the day before day 0 is day -1, and two days before day 0 is day -2. After the transplant days are counted as positive days, such as day +1 is the day after the transplant.

**Pre-Transplant Preparative (Conditioning) and Immune Suppression Regimen:**
All drugs used as part of this treatment plan are commercially available and routinely used in transplantation of blood, marrow and umbilical cord blood.

The preparative regimen consists of chemotherapy (cyclophosphamide and fludarabine) and total body irradiation (TBI) to make room in your bone marrow for the donor cells to grow. It may also kill remaining cancer cells. Depending on your previous treatment history you also may receive the standard drug ATG.

You will be given two drugs to reduce the risk of graft-versus-host disease (GVHD) as standard preventive care. Both drugs come in an oral (by mouth) form, but mycophenolate mofetil (MMF) may initially be given through the central line (intravenously). The first drug, sirolimus will be continued for approximately 6 months, although its dose may slowly be decreased beginning at 3 months after transplant. The second drug, MMF will continue for approximately 1 month after transplant.

Other drugs and intravenous fluids will be given during the preparative regimen to reduce or prevent side effects. Some of these are detailed in the risk section later in this consent.

**Umbilical Cord Blood (UCB) Cell Infusion:**
On the day of the transplant (day 0), you will receive the UCB cells as an infusion similar to a blood transfusion. If you are receiving more than one UCB unit, they will be given as separate infusions within 30 to 60 minutes of each other.

**Blood Count Recovery and Follow-Up:**
You will remain in the hospital until your blood counts have recovered to a safe level for discharged. You will continue to be followed in the clinic at least weekly for the first 1 to 3 months after transplant.

Once your blood counts are good and you have recovered from the effects of the transplant, you will be seen at 3, 6, 12 and 24 months after the transplant. At each of these visits you will have a physical exam and blood work done. A bone marrow test and imaging studies may be performed for reassessment based on your specific disease. Additional visits may be required based on individual needs. Follow-up after 24 months (2 years) will continue at least yearly.

## Risks of Receiving a Transplant

You are at risk of having side effects and the side effects may vary in severity. The severity may be mild, moderate or severe, including death. Any symptoms or conditions that you have before you start study treatment may get worse. Many of the side effects overlap and are difficult to identify the cause.

A detailed description of these risks is part of the appendix to this consent form. The most serious and frequent risks of transplant include but are not limited to:

- tumor lysis syndrome,
- stem cell infusion reactions
- immunological reaction between donor cells and your normal tissues called graft vs host disease
- marrow aplasia and failure to engraft
- in case you become pregnant, risk of fetal malformations
- damage to vital organs

- serious infections
- infertility and sterility
- recurrence of your disease

If you have any additional questions about any of these risks you should ask your doctor about them.

**Benefits of Study Participation**

The information learned in this study will add to our knowledge of hematologic malignancies and the use of transplant.

**Alternatives to Study Participation**

Participation in this study is voluntary.

You may choose to not participate in this study. Other options may include:

- investigational treatments that may or may not include transplantation at this institution or at other research centers
- comfort care only, where treatment is directed only at reducing symptoms, relieving suffering, and maximizing comfort, dignity, and control. In comfort care only, treatment is not directed at curing, slowing, or reversing your disease.
- outside of this clinical protocol, you could receive a similar treatment (chemotherapy and cord blood transplant) at our center, but we would not be collecting data on your outcomes.

Your doctors can tell you more about your condition and the possible benefits of the different available treatments.

**Study Costs**

All treatment and care in this study is standard of care. You and your 3rd party payer (health insurance) will be responsible for all costs associated with the transplant procedures, including the cost of the umbilical cord blood unit(s), all laboratory tests, the preparative therapy, medications to prevent/reduce side effects, the hospitalization and follow-up clinic visits.

You will receive no monetary compensation for participation in this study.

**Research Related Injury**

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your 3rd party payer. If you think that you have suffered a research related injury let your doctor know right away.

**Confidentiality**

The records of this study will be kept private. Information will be kept in your medical record and in study case report forms. Information gained from this study will be used for research and educational purposes. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- Departments at the University of Minnesota with research oversight
- The Masonic Cancer Center at the University of Minnesota and/or their designee
- National and international transplant registries including the Center for International Blood and Marrow Transplant Research (CIBMTR) and National Marrow Donor Program (NMDP)
- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people

To this extent, confidentiality is not absolute.

A description of this clinical trial is available on www.ClinicalTrials.gov as required by U.S. law. This web site will not include information that can identify you. You may search this web site at any time.

**Protected Health Information (PHI)**

Your PHI created or received for the purposes of this study is protected under the federal regulation known as HIPAA. Refer to the attached HIPAA authorization for details concerning the use of this information.

**Voluntary Participation**

Taking part in this study is your choice. You may choose either to take part or not to take part in the study.

If you decide to take part in this study, you may leave the study at any time and we will stop collecting data; however if you no longer want to be treated, let your doctor know so he or she can tell you how to stop safely. Stopping treatment after the preparative regimen without out receiving the UCB infusion could result in death.

No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You may still get your medical care from this institution.

**New Information**

You will be told about new information or changes in the study that may affect your health or your willingness to continue in the study.

**Contacts and Questions**

The physicians involved in your care are available to answer any questions you may have concerning this treatment. In addition, you are encouraged to ask questions concerning this study that you may have in the future. If you have any questions concerning this particular study, you may contact the principal investigator of the study, Dr. Margaret MacMillan at 612-626-2961.

This research has been reviewed and approved by an IRB within the Human Research Protections Program (HRPP). To share feedback privately with the HRPP about your research experience, call the Research Participants' Advocate Line at 612-625-1650 (Toll Free: 1-888-224-8636) or go to z.umn.edu/participants. You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
  You have questions about your rights as a research participant.
  You want to get information or provide input about this research.

If you choose to participate, you will be given a signed copy of this form to keep for your records.

**Signature**

I have read it or it has been read to me. I have had my questions answered. I agree to take part in this study.

_____
Printed name of the subject

_____ _____
Signature of subject Date

_____
Printed name of the researcher obtaining consent

_____ _____
Signature of the researcher obtaining consent Date

IF USING A SHORT FORM TO CONSENT, THE WITNESS SIGNATURE BLOCK MUST BE COMPLETED BELOW:

**WITNESS STATEMENT:**
The participant was unable to read or sign this consent form because of the following reason:

☐ The participant is unable to read the information
☐ The participant is visually impaired
☐ The participant is non-English speaking
☐ The participant is physically unable to sign the consent form. Please describe:

_____
☐ Other (please specify):

_____

**For the Consent of Non-English Speaking Participants when an Interpreter is Used:**

As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

_____ _____

Signature of Interpreter Date

_____

Printed Name of Interpreter

OR:

**Statement from a Non-Interpreter:**
As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

_____ _____

Signature of Individual Date

_____

Printed Name of Individual

## Signature Block for Adult Unable to Consent:

Your signature documents your permission for the named participant to take part in this research.

_____
Printed Name of Participant

_____ _____
Signature of Legally Authorized Representative Date

_____ _____
Printed Name of Legally Authorized Representative Date

_____ _____
Signature of Person Obtaining Consent Date

_____ _____
Printed Name of Person Obtaining Consent Date

## Appendix A - Risks of Transplantation

**Risks Associated with a Transplant:**

**Stem Cell Infusion Reaction:** The umbilical cord blood stem cells are given in a manner similar to a blood transfusion, and as with a blood infusion there is a small risk of an allergic reaction to the cells as they are given. This may include changes in heart rate or rhythm, changes in blood pressure, fever, chills, sweats, nausea/vomiting, diarrhea, abdominal cramping, and headache. Medications are given before the cell infusion to reduce the risk of an allergic reaction. If during the infusion symptoms develop, the rate of the infusion may be slowed or stopped and/or additional medications given to reduce the intensity of any reactions.

**Graft versus Host Disease:** (also called GVHD) is caused by donor (or graft) cells attacking the patient's (recipient or host) body. GVHD can occur either within the first 3 months after the transplant (acute GVHD) or later, usually 4 or more months after the transplant (chronic GVHD).

Acute GVHD commonly involves the skin, liver, and the intestines with symptoms such as a skin rash, jaundice (yellowing of the skin), nausea, vomiting and diarrhea. The treatment of acute GVHD may require high doses of cortisone-like drugs (methylprednisolone or prednisone)

Chronic GVHD usually involves the skin, liver, eyes, glands and joints with symptoms such as skin rash and thickening, jaundice (yellowing of the skin), dry mouth or/eyes, hair loss, dental decay, weakness or a pain and tightening around the joints, muscle cramps, shortness of breath. Chronic GVHD may be mild and respond to drugs which suppress the immune system, or it could be very severe; it may also last for several years.

To reduce the chance of developing GVHD, two drugs, sirolimus and MMF will be given starting on day -3. Both drugs come in an oral (by mouth) form. Sirolimus is taken daily for approximately 6 months. Mycophenolate mofetil (MMF) is stopped around the time of discharge from the hospital. If GVHD occurs, standard GVHD therapy is given.

**Marrow Aplasia (Suppression of the Bone Marrow):** All patients will have low blood counts from the chemotherapy, but are expected to normalize within a few weeks after the transplant. You may receive a daily injection of G-CSF continuing until the white count begins to recover. Risks of G-CSF are listed below. Marrow aplasia and failure to engraft are names used to describe when blood counts do not recover as expected.

Symptoms of marrow aplasia include increased risk of bleeding and/or bruising due to low platelets, increased risk of infection due to low white blood cell count, and shortness of breath and tiredness as a result of anemia due to low red blood cell count. Marrow aplasia is treated with blood transfusions and growth factor (which stimulates bone marrow cells), and other precautions. Severe or prolonged aplasia (lasting more than 1 month) can lead to death, usually from infection. If the bone marrow does not recover, sometimes it can be corrected by another stem cell transplant; however not all patients are able to have another transplant.

**Damage to the Vital Organs:** Any organ may be damaged by the intensive transplant treatments.

Some patients will experience severe lung problems due to a reaction to the transplant treatments or infections such as cyomegalovirus (CMV) and/or a reaction of the lungs to the chemotherapy. Although treatments are available for this type of pneumonia, interstitial pneumonia can be fatal.

Some patients will suffer veno-occlusive disease of the liver (VOD), a complication that may result from high doses of chemotherapy and/or radiation. Patients who have VOD become jaundiced (yellowish skin), have liver function abnormalities, abdominal swelling, and abdominal pain. Although some patients recover, these complications may result in organ failure and permanent damage, or even death.

**Serious Infections**: Recovery of the immune system may take many months following the initial recovery of the white cell count. During this time, there is an increased risk of infections. Medications to reduce the risk of developing an infection are prescribed during

this time; however, preventative treatments are not always effective. If an infection develops, discharge from the hospital may be delayed or re-hospitalization required. Infections can be fatal.

**Sterility and Future Childbearing Potential for Men and Women:** Chemotherapy may affect fertility. Male patients may become sterile (unable to produce sperm). Female patients may find that their menstrual cycle becomes irregular or stops permanently. Damage to reproductive tissue may result in birth defects or permanent inability to father a child or become pregnant. These risks and options will be discussed in detail with the medical staff before beginning treatment. However, PREGANCY CAN OCCUR, and an effective method of birth control must be used by sexually active men and women.

**Risk to the Unborn:** These treatments are NOT safe at any stage of pregnancy. Therefore, pregnant and nursing women are not eligible for this study.

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

**Risks Associated with Umbilical Cord Blood (UCB) as a Stem Cell Source:**

**Genetic disease within the cord blood cells:** It is possible that certain genetic diseases (for example thalassemia or Gaucher's disease) may be passed through the transplanted umbilical cord blood cells. While these diseases are very rare, each umbilical cord blood unit can only be tested for a few of the many possible genetic diseases. To reduce this possibility further, cord blood is not collected from babies with a known history of genetic diseases.

**Incorrect labeling of the UCB units:** Though extremely unlikely, it is possible that incorrect labeling of an umbilical cord blood unit could occur. In this event, the transplant may be delayed for several hours while the UCB unit is typed (check to see if it is a correct match). Should the typing be incorrect, the transplant will be delayed until an alternative source of cells is located.

## Appendix B – Side Effects of Study Drugs and TBI

If you are not on **allopurinol** at the time of study enrollment, you will be started on it to prevent tumor lysis syndrome, a potential complication of any leukemia or lymphoma treatment when too many cancer cells die at once overwhelming the body's ability to process them.

### Preparative (Conditioning) Regimen:

| **Cyclophosphamide** | | |
|---|---|---|
| **common** (occuring in 30 or more out of every 100 persons) | **less common** (occuring in fewer than 30 but more than 5 out of 100 persons) | **rare, but may be serious** (occuring in 5 or fewer out of 100 persons) |
| • low white blood cell count with increased risk of infection<br>• hair loss or thinning, including face and body hair (usually grows back after treatment)<br>• nausea<br>• vomiting<br>• loss of appetite<br>• sores in mouth or on lips<br>• bleeding from bladder, with blood in urine<br>• diarrhea<br>• long-term or short-term infertility (inability to have children) in women and men | • low platelet count (mild) with increased risk of bleeding<br>• darkening of nail beds<br>• acne<br>• tiredness<br>• infection<br>• fetal changes if you become pregnant while taking cyclophosphamide | • heart problems with high doses, with chest pain, shortness of breath, or swollen feet<br>• severe allergic reactions<br>• skin rash<br>• scarring of bladder<br>• kidney damage (renal tubular necrosis) which can lead to kidney failure<br>• heart damage, with trouble getting your breath, swelling of feet, rapid weight gain<br>• scarring of lung tissue, with cough and shortness of breath<br>• second cancer, which can happen years after taking this drug<br>• death from infection, bleeding, heart failure, allergic reaction, or other causes |

You will receive the drug **Mesna** and additional intravenous fluids before, during and after the cyclophosphamide to reduce the risk of bladder damage. The most common risks of Mesna include nausea, vomiting, tiredness, headache, pains in your legs and arms and an unpleasant taste in your mouth.

| **Fludarabine** | | |
|---|---|---|
| **common** (occuring in 30 or more out of every 100 persons) | **less common** (occuring in fewer than 30 but more than 5 out of 100 persons) | **rare, but may be serious** (occuring i 5 or fewer out of 100 persons) |
| • low white blood cell count with increased risk of infection<br>• low platelet count with increased risk of bleeding<br>• low red blood cell count (anemia) with tiredness and weakness<br>• tiredness (fatigue)<br>• nausea<br>• vomiting<br>• fever and chills<br>• infection | • pneumonia<br>• diarrhea<br>• loss of appetite<br>• weakness<br>• pain | • numbness and tingling in hands and/or feet related to irritation of nerves<br>• changes in vision<br>• agitation<br>• confusion<br>• clumsiness<br>• seizures<br>• coma<br>• cough<br>• trouble breathing<br>• intestinal bleeding<br>• weakness<br>• death due to effects on the brain, infection, bleeding, severe anemia, skin blistering, or other causes<br>• death from infection, bleeding, heart failure, allergic reaction, or other causes |

| **Total Body Irradiation (TBI)** | | |
|---|---|---|
| **common** (occuring in 30 or more out of every 100 persons) | **less common** (occuring in fewer than 30 but more than 5 out of 100 persons) | **rare, but may be serious** (occuring in 5 or fewer out of 100 persons) |
| • nausea and vomiting<br>• diarrhea<br>• cataracts<br>• sterility<br>• hyperthyroidism, hypothyroidism or other hormone problems<br>• growth failure<br>• intestinal cramps<br>• mucositis | • parotitis (swelling of the gland located under the jaw bone)<br>• interstitial pneumonitis (inflammation of the air sacs of the lung)<br>• generalized mild erythema<br>• veno-occlusive disease (blockage of the very small (microscopic) veins in the liver causing enlargement of the liver)<br>• pericarditis (inflammation of the lining around the heart) | • dysphagia (difficulty swallowing)<br>• vertebral deformities<br>• nephropathy (kidney damage)<br>• risk of 2nd malignancy years later |

| **Total Body Irradiation (TBI)** | | |
|---|---|---|
| **common** (occuring in 30 or more out of every 100 persons) | **less common** (occuring in fewer than 30 but more than 5 out of 100 persons) | **rare, but may be serious** (occuring in 5 or fewer out of 100 persons) |
| | • cardiomyopathy (damage to the heart muscle) | |

| **Anti-Thymocyte Globulin (ATG) –** Your Doctor Will Tell You if You Are to Receive This Drug | | |
|---|---|---|
| **common** (occuring in 30 or more out of every 100 persons) | **less common** (occuring in fewer than 30 but more than 5 out of 100 persons) | **rare, but may be serious** (occuring in 5 or fewer out of 100 persons) |
| • fever<br>• chills<br>• low white blood cell count with increased risk of infection<br>• low platelet count with increased risk of bleeding<br>• pain<br>• headache<br>• abdominal pain<br>• diarrhea<br>• high blood pressure (hypertension)<br>• nausea<br>• swelling of hands and/or feet (peripheral edema)<br>• shortness of breath (dyspnea)<br>• loss or lack of strength (asthenia)<br>• high levels of potassium in the blood (hyperkalemia)<br>• rapid heartbeat (tachycardia) | • feeling poorly (malaise)<br>• dizziness | • severe allergic reaction (anaphylaxis) |

It is also possible that the addition of antithymocyte globulin (ATG) may increase the risk that certain viruses, like EBV which causes mononucleosis, may reactivate in those previously exposed to the virus before transplant.

## G-CSF (Given to Reduce Risk of Marrow Suppression of the Bone Marrow):

| G-CSF | | |
|---|---|---|
| **common** (occuring in 30 or more out of every 100 persons) | **less common** (occuring in fewer than 30 but more than 5 out of 100 persons) | **rare, but may be serious** (occuring in 5 or fewer out of 100 persons) |
| none | • bone or muscle pain<br>• injection site reaction (redness, pain, or swelling) | • allergic reaction<br>• spleen enlargement or rupture –symptoms of an enlarged spleen include a feeling discomfort, fullness, or pain on the upper left side of the abdomen; this pain may spread to the left shoulder<br>• serious lung problems (ARDS)<br>• coughing up blood |

## Drugs Given To Reduce The Risk of GVHD:

| Mycophenolate Mofetil (MMF) | | |
|---|---|---|
| **common** (occuring in 30 or more out of every 100 persons) | **less common** (occuring in fewer than 30 but more than 5 out of 100 persons) | **rare, but may be serious** (occuring in 5 or fewer out of 100 persons) |
| • miscarriage<br>• birth defects<br>• diarrhea<br>• damage to unborn baby<br>• limited effectiveness of birth control<br>• stomach pain<br>• upset stomach<br>• vomiting<br>• headache<br>• tremors<br>• low white blood cell count with increased risk of infection<br>• increased blood cholesterols<br>• swelling of the hands, feet, | • anemia<br>• rash<br>• difficulty falling asleep or staying asleep<br>• dizziness<br>• uncontrollable hand shakes | • difficulty breathing<br>• unusual bruising<br>• fast heartbeat<br>• excessive tiredness<br>• weakness<br>• blood in stool<br>• bloody vomit<br>• change in vision<br>• cancers, such as lymphoproliferative disease or lymphoma<br>• progressive multifocal leukoencephalopathy – a disorder of the brain with a variety of symptoms including muscle weakness, difficulty with speaking and/or |

| **Mycophenolate Mofetil (MMF)** | | |
|---|---|---|
| **common** (occuring in 30 or more out of every 100 persons) | **less common** (occuring in fewer than 30 but more than 5 out of 100 persons) | **rare, but may be serious** (occuring in 5 or fewer out of 100 persons) |
| ankles or lower legs | | movements |

## For Females of Child Bearing Potential taking MMF:

1. MMF could be damaging to an unborn baby if you are pregnant or become pregnant while receiving the drug.

2. MMF can limit the effectiveness of birth control pills and thus increase your chances of becoming pregnant while taking it.

| **Sirolimus** | | |
|---|---|---|
| **common** (occuring in 30 or more out of every 100 persons) | **less common** (occuring in fewer than 30 but more than 5 out of 100 persons) | **rare, but may be serious** (occuring in 5 or fewer out of 100 persons) |
| • chest pain, feeling weak or tired<br>• pale skin, easy bruising or bleeding, weakness<br>• fever, chills, body aches, flu symptoms<br>• night sweats, weight loss<br>• swelling of face, stomach, hands or feet<br>• pain or burning when urinating<br>• slow healing of a wound<br>• joint pain<br>• nausea, vomiting, diarrhea, constipation, stomach pain<br>• headache<br>• acne or skin rash<br>• high triglycerides and cholesterol | • fast heart rate<br>• coughing up blood or mucus<br>• rapid weight gain | ▪ pain when breathing, feeling short of breath<br>▪ feeling like you might pass out<br>▪ Increased susceptibility to infection and the possible development of lymphoma and other malignancies may result from immunosuppression |