Informed Consent for Research

HAPNK1 TRANSPLANT RECIPIENT

HAPLOIDENTICAL DONOR HEMATOPOIETIC PROGENITOR CELL AND NATURAL KILLER CELL TRANSPLANTATION WITH A TLI BASED CONDITIONING REGIMEN IN PATIENTS WITH HEMATOLOGIC MALIGNANCIES

NOTE*: When we say "you" in this document, we mean "you or your child."*

We are asking you to take part in a research study. You are being invited to join this study because you have a type of cancer affecting the blood or lymphatic system that is difficult to treat. At this time, the cancer has either 1) disappeared (remission), 2) come back (relapsed) or, 3) not responded well (refractory) after very intensive therapy. The research study will be discussed with you. After you have learned about the study, you are to read this consent form. It also explains the research study and how your participation might be involved. You are encouraged to ask questions at any time while you are learning about the research study. If you agree to take part in the research study, we will ask you to sign this consent form. We will give you a copy to keep for future reference

Before you learn about the study, it is also important that you know the following:

- Whether or not you take part in this study is entirely up to you.
- You may take time to consider whether or not you would like to take part in this study and any options that are available to you.
- The person in charge of the study (called the principal investigator and researcher) is Dr. Brandon Triplett. This doctor may be reached by phone at 901-595-3300. Please feel free to call him if you have questions at any time.
- If you choose not to be in the study, or to leave the study at any time, you may still be able to get routine medical care at St Jude.
- You may choose to receive other treatment(s) for your disease, if any are available.
- This study is being sponsored by and conducted at St. Jude Children's Research Hospital.

Why is this study being done?

Your doctors are proposing to treat you with an allogeneic stem cell transplant. An allogeneic stem cell transplant means that the stem cells used for the transplant are obtained from someone other than you.

The purposes of this study are the following:

1. To study the rate of engraftment for participants who receive this study transplant procedure.
2. To study how many participants who receive this study transplant procedure experience relapse of their disease.

3. To find out the effects (good and bad) of this procedure on the research participants.
4. To study how often participants who receive this study procedure develop GVHD.
5. To learn more about how the immune system (infection fighting system) develops and works for participants who receive this study transplant procedure.

Before you learn about this study procedure, you need to be aware that there are many risks with stem cell transplantation. The side effects of any type of stem cell transplant can be severe and life threatening, and may even cause death. There is no promise that you will survive the transplant or be cured of your disease. It is important that you understand the possible risks and benefits before you agree to this treatment.

You also need to be aware that taking part in this study will significantly change your normal daily activities and quality of life. These activities include play, socializing (spending and enjoying time with friends), work, diet and sleep. Many side effects of stem cell transplant may also negatively affect your energy, mood, and general well-being. You and an adult caregiver will need to stay in or near Memphis for at least 80 to 100 days after this transplant and return to St. Jude for frequent follow-up visits for several years.

This change in quality of life may be long and drawn out. It is important that you speak with your doctor about these quality of life issues when compared to other treatment choices, such as medical therapy alone without transplantation, supportive therapy (such as transfusions for low blood counts and antibiotics for infections), or hospice treatment (supportive, comfort care for persons with terminal illnesses).

General Overview of this Haploidentical Donor Transplant Study Procedure

Treatment for your disease includes stem cell transplantation. Standard stem cell transplantation starts with giving you radiation and/or chemotherapy to damage or kill your bone marrow. Bone marrow is mostly located in the large bones of the body like the hips and the leg bones. By damaging or killing your bone marrow, room is made within the bones – called the “bone marrow space.” You then get stem cells from the bone marrow of another person called the “donor.” Donor stem cells are needed in order to restore and “rebuild” your bone marrow that has been damaged by the chemotherapy and to give you new bone marrow. Your new bone marrow will help you build healthy immune and blood cell forming systems. The donor stem cells (called “the graft”) travel through your blood to the bone marrow space and begin to grow and make new blood cells. Giving (infusing) you the stem cell graft is called “a stem cell transplant.”

The best type of donor for a stem cell transplant is a brother or sister who is a "match" for the patient's immune type (HLA type). You do not have a suitable or available matched brother or sister to be the donor for this transplant. Other types of donors that can be used are closely matched, unrelated volunteer donors, or partially matched family member donors. An available and suitable closely matched unrelated volunteer donor has not been found, or is not available in the necessary time. Therefore your doctors are proposing to use a partially matched family member donor (haploidentical) for your transplant.

Stem cells from a haploidentical donor will not be as closely matched as those from a matched brother or sister or from a matched unrelated volunteer. As a result, there is a higher chance of problems related to the stem cell transplant. Such problems include failure of the donor cells to grow (graft failure), and a condition called graft-versus-host disease (GVHD). GVHD occurs when the donor cells (the graft) recognize that the body tissues of the patient (the host) are different. Severe GVHD can be life threatening. Because of these potential problems, you will not receive all of the blood cells from you donor. Instead you will receive certain populations of blood cells, including blood making cells, memory T cells, and natural killer cells. It is important for you to know that you have the right to review your HLA typing and the HLA typing of the donor providing the cells for your transplant.

What are other options to being in this study?

Other options to taking part in this research study are:

1. Continue to receive standard chemotherapy without stem cell transplant
2. Experimental treatments using new drugs or methods, if available.
3. Supportive care (such as transfusions for low blood counts, medications for pain, antibiotics for infections or hospice care for patients with terminal illness).
4. No further treatment.

The researcher in charge of the study can tell you about the disease and the benefits of other treatment options. Please feel free to ask the researcher about the disease and its outcomes. You need to be aware that if you decide not to get more treatment, the disease will get worse.

How many research participants will take part in this study?

We expect that about 75 transplant recipients and 75 transplant donors will take part in this study over a period of about six years.

What will be done in this study?

This treatment has the following parts, which are explained below this list:

- Conditioning treatment (radiation treatment and chemotherapy)
- Stem cell collection from a partially matched family member donor
- Stem cell processing
- Stem cell infusion
- NK cell collection
- NK cell processing
- NK cell infusion

1. <u>Conditioning treatment – radiation and chemotherapy</u>

Conditioning treatment is the treatment that is given to get the body ready to accept the donor stem cells. Total lymphoid radiation (TLI) and high dose chemotherapy will be given before the stem cell transplant to further damage your immune system and help to kill the bone marrow. Damaging your bone marrow will help to provide room within your bone marrow space for the new donor stem cells to settle and grow. You will be given four chemotherapy drugs. The names of these drugs are fludarabine, cyclophosphamide, thiotepa and melphalan. Each of these medications will be given by vein. On "day 0" you will have the stem cell infusion. The table below outlines the treatment you will receive.

Treatment Table:

Medication Name	**Schedule**
Total lymphoid irradiation (TLI)	Days -9, -8 and -7
Fludarabine (a chemotherapy)	Days -8, -7, -6, -5 and -4
Cyclophosphamide (a chemotherapy)	Day -6
Thiotepa (a chemotherapy)	Day -3
Melphalan (a chemotherapy)	Days -2 and -1
Stem cell transplant infusion (Infusion #1 of 2)	Day 0
Stem cell transplant infusion (Infusion #2 of 2)	Day +1
NK cell infusion	Day +6

The minus sign (-) means before transplant. Day 0 is the day of transplant. The plus sign (+) means after transplant.

You will receive a medication called mycophenylate mofetil (MMF) to help reduce the risk of GVHD. MMF will be given by vein starting one week after the NK cell infusion. As soon as you are able to tolerate oral (by mouth) medicine, MMF may be provided in a pill or liquid form. You will continue to take MMF for about 1 month and then over the next few weeks it will be slowly decreased ("weaned").

You will be monitored closely during treatment. You will be given other medicines to help lessen the side effects as much as possible. The days and length of these treatments may vary depending on how your body responds to the medications and if there are any side effects from the medicines or treatment. Your doctor will discuss any needed changes in this treatment and related medicines with you.

2. Stem cell collection from a partially matched family member donor**.** You will receive stem cells collected from the blood of a partially matched family member donor through a procedure called apheresis. A full description of this apheresis procedure will be given to the donor in a separate consent form for his/her review and signature. The donor's stem cells

will typically be collected the day before you receive each infusion of the transplant. These stem cells will be given soon after the processing and filtering has been completed. Sometimes, the stem cell infusions need to be delayed (not given on the planned days) requiring that the donor stem cells be frozen and stored in a St. Jude laboratory before infusing; however, this is rare.

The stem cells may need to be collected from the bone marrow of the donor through a surgical procedure called a bone marrow harvest. This would be done for example if the donor is unable to provide enough stem cells for the transplant through his/her blood. This is also rare. If donor bone marrow is used, it will be processed in the same way as the blood stem cells.

3. Stem cell processing. The family member donor stem cells will be processed on the CliniMACS system. The CliniMACS has not been licensed for use in the United States. Therefore, using this machine for stem cell processing is considered experimental and may result in unknown risks. The first collection of donor's cells will be placed on the CliniMACS device where the system will select or "enrich" the graft with as many stem cells as possible, while removing all other blood cell populations. When processed, the graft, which contains the stem cells will typically be infused fresh the same day, but may be frozen until the recipient is ready for transplant. A second collection of donor's cells will be placed on the CliniMACS device where the system will remove or deplete cells that have a molecule called CD45RA. This will remove naïve T cells thought to be the primary cause of GVHD, and leave memory T-cells which have activity against infections, and may have activity against your cancer. Using this machine for mismatched family donor processing is considered experimental and could result in unknown risks.
4. Stem cell infusion. You will receive the donor stem cells by vein (the transplant). This infusion of stem cells will take place in your patient room. We expect the transplant to be given in two infusions, once per day taking about 30 minutes each. The first day of infusion is called Day 0 and the second infusion day is called Day +1.

   Once in the bloodstream, the stem cells will go through your blood to the bone marrow space and should begin to grow.
5. NK cell collection from a donor. NK cells will be collected from the family member donor who signed a separate consent form for the stem cell and NK cell collection. NK cells will be drawn from the blood of the donor.
6. NK cell processing and selection. NK cells collected from the donor contain T cells that can cause GVHD. For the NK cell processing, we will also use the CliniMACS system to remove the T cells. Again, the FDA has not licensed the CliniMACS for use in the United States. Therefore, using this machine for NK cell processing is also considered experimental and could result in unknown risks.
7. NK cell infusion. You will receive the donor NK cells by vein on or about Day +6.
8. Donor lymphocyte infusion (if needed). We will monitor the number of donor cells in your blood each week after the stem cell transplant for about 15 weeks (100 days). The number should increase as the stem cells begin to grow in the bone marrow. If the number of donor cells in the blood is lower than needed, we will give you another type of blood cell from the

donor. These donor blood cells are called lymphocytes. Lymphocytes are white blood cells that are given to increase the number of donor cells in your body. These donor lymphocytes may also be processed by removing the cells with the molecule CD45RA when indicated. In some cases, you may be given additional low dose chemotherapy at the time you receive the donor lymphocytes.

You will be in the hospital for about 4 to 8 weeks. How long you are in the hospital will depend on how fast the stem cells grow back, if there are any complications such as infection, and how severe the complications are. We will monitor you closely, both while the stem cells engraft (grow and begin to work) and for the first 3 to 4 months after the transplant. During this time, you and an adult caregiver will need to stay in or near Memphis for frequent clinic visits even after discharge.

What routine tests will be done?

Your doctors have already reviewed your medical history, clinical status and determined you are eligible and prepared to have a stem cell transplant. This evaluation has included but was not limited to blood tests, kidney, heart and lung function tests. Before this treatment starts, your doctor will recheck many of these tests and conduct another complete physical examination to make sure you continue to be able to have this type of treatment.

Before, during and after this treatment, blood tests, bone marrow tests and radiological scans (for example – chemistries, CBCs, immune cell surveys, immunoglobulins, minimal residual disease (MRD), chest X-rays, bone scans, MRIs) will be done to evaluate your condition and the effects (good and bad) of the treatment on your body and disease. These tests are the same tests and follow-up tests used for all patients who receive stem cell transplants from allogeneic donors (donors other than themselves). At first these tests will be done often, but will then be done less often as your condition gets better.

What research tests or special studies will be done?

Special immune studies and disease evaluations will be checked at specific time points during this study. These blood tests will look at how your body's infection fighting system is growing and how well it is working.

Special immune studies to be collected on this study	Blood volume totals for length of study	Frequency of sample collections during this study
Thymic output and T cell repertoire	4 samples total Volume = about 3 teaspoonful for each sample	Pre-transplant, Months 3, 6 and 12
T cell and NK cell number and function	6 samples total Volume = about 3 teaspoonful for each sample	Pre-transplant, Months 1, 2, 3, 6 and 12

Immunophenotype evaluations	About 6 teaspoons	Pre-transplant and months 1, 2, 3, 6 and 12 after transplant
T cell function studies	About 7 teaspoons	Pre-transplant and months 1, 2, 3, 6 and 12 after transplant

How long will I be in the study?

The total length of the treatment and follow-up for this study is one year. Patients who receive a stem cell transplant at St. Jude are asked to return to the Transplant Clinic for doctor visits and follow-up evaluations at least once a year (annually) for at least 10 years to see if any long term effects of this research treatment occur. For the purpose of this study, you will need to be followed for 1 year after this transplant. After one year you will be asked if you would like to join a long-term follow-up study (BMTFU) of children and young adults who have received a stem cell transplant at St. Jude Children's Research Hospital.

Can I be taken out of the study without my consent?

You may be taken off the treatment without your consent for the following reasons:

- Your doctor decides that continuing in this study would be harmful.
- You need a treatment not allowed on this study.
- You are unable to keep appointments or take medicines as instructed.
- Your condition gets worse.
- You have a positive pregnancy test.
- New information is learned that a better treatment is available, or that the study is not in your best interest.
- The donor stem cells do not grow in your body or are rejected.
- Your donor develops a change in health status, which would result in his/her inability to donate stem cells needed for the primary stem cell study infusion or any additional infusions.

What happens if I leave this study?

You can stop or withdraw from this study at any time. However, the risk to you is much greater, possibly life-threatening and fatal (cause death) if you withdraw *after* starting the conditioning treatments (radiation, chemotherapy) but *before* the donor stem cells have been infused or settled in your bone marrow space. If you decide to withdraw from the study, you should talk to your doctor first. Your doctor can recommend other treatment options if you stop the study treatment or if the treatment is stopped without your consent.

What are the risks of the study?

Both your disease and its prior treatment may be associated with potentially life-threatening complications, side effects, or death. The main risks of this treatment are the side effects of stem cell infusion and of the drugs used for conditioning before and after the infusion. There is also a

chance that you could die from side effects of the study treatment, such as infection, failure of the donor cells to grow, or graft-versus-host disease. The treatment can cause some, or all of the side effects listed below. There may also be side effects that we cannot predict.

Because the CliniMACS device is being used for each of the cell infusions, and it is considered experimental, there may be risks including possible life-threatening reactions, which we do not know about right now. Since only a small number of children and young adults in the world have received this study treatment, we cannot be certain about all the possible risks.

Filtering and processing of the stem cells and NK cells using the CliniMACS device.

Small amounts of mouse proteins and iron particles are added to the donor blood cells to help with the processing. If you are allergic to these materials, you could have a severe reaction when the donor cells are infused. This reaction could include fever, chills, wheezing, difficulty breathing, hives, skin rashes, severe low blood pressure, or death. Joint pain and fever often happen about 24 to 48 hours after beginning the donor cell infusion. You should tell the doctors and nurses if you have a history of asthma, active inflammatory disease, allergies, or have ever had any exposure to mouse protein. It is possible that you could still have an allergic reaction when the donor cells are infused, even if you do not have a history of allergies to these substances.

There is a small chance that germs or yeast could get into the donor blood cells during CliniMACS processing. This could cause an infection in your body after the donor cells are given. We will make every effort to keep the donor cells sterile (free of germs and yeast), and we will test for germs and yeast in the cells. However, we cannot guarantee that all possible germs and yeast in the blood will be found. You will receive antibiotics and anti-yeast medicines as part of this therapy, if necessary. The risk of developing a severe infection from germs or yeast due to the donor cells is low.

Side effects of donor stem cell infusion.

The infusion of stem cells may cause blockage of the blood vessels in the lungs, kidney damage, trouble breathing, or failure of marrow to grow and make normal blood cells. There is also a small risk (less than 1 in 100) that the donor stem cells may contain a bacteria or virus that could cause an infection. The stem cell infusion will be checked for bacteria, and if there is any sign of infection, you will be treated with appropriate antibiotics.

Risks related to frozen stem cell product infusion (if needed)

As noted before, sometimes the donor stem cell product may need to be frozen and stored until the transplant recipient is ready for the infusion. A frozen product is thawed (warmed at room temperature to "unfreeze") just before the infusion. When the donor cells are collected, some fluids and a chemical called Dimethyl sulfoxide (DMSO) must be added to protect the cells during the freezing process. If a frozen product is needed and infused, the DMSO in the frozen cells may cause you to have a temporary strange taste and smell. You may be able to eat things like candy, ice cream or popsicles to cover this taste during and/or after the infusion. DMSO may possibly cause the blood pressure to go up, nausea, and vomiting. In very rare cases it may cause the blood pressure to drop, cause changes in the heartbeat, or an allergic reaction. Your urine may have a red color for a few hours. This is from the lysed (broken up) red blood cells

that are not protected during the freeze and thaw process. These effects usually last only a short time and, in almost every case, can be treated.

Risks for infection.

You will have a damaged bone marrow and immune system until the new donor cells have grown and begin to function (engraft). During this time you will be at risk of infection, which can be life-threatening in 5% to 10% of patients. We will give medicines to reduce this risk. Most infections can be treated with antibiotics. Sometimes an infection, usually from a virus, cannot be treated. In some cases, patients die of infection.

Graft-versus-host disease.

Graft-versus-host disease, or GVHD, is a serious and sometimes fatal side effect of stem cell infusion. GVHD occurs when the donor cells recognize that your body tissues are different. When this happens, donor cells will attack your body, mainly the skin, liver and intestines. Stem cell processing as noted above is being provided in this treatment in an effort to decrease the risk of GVHD. If you develop GVHD, the doctors will discuss treatment options for this disease with you. GVHD can occur early after transplant (usually the first 100 days) and is called acute GVHD. Eighteen of the first 54 patients on this protocol have developed acute GVHD (one grade 1, three grade 2, nine grade 3, and five grade 4). It often affects the skin, liver, and gut. GVHD can also occur late (after 100 days) and is called chronic GVHD. Twelve of the first 54 patients on this protocol have developed chronic GVHD (5 mild, 5 moderate and 2 severe). It may occur in any organ. Both acute and chronic GVHD can occur with this treatment and may be very mild to severe (life threatening). Most patients with GVHD responded fully to treatment.

There are also other conditions that occur when a person's immune system reacts abnormally against medications or infection. These conditions are typically rare, but can be severe (life threatening) and may be more likely to occur in transplant recipients. Three of the first 26 patients on this protocol developed these types of conditions.

Graft failure/ Graft rejection.

The donor stem cells may not grow in your body. This is called graft failure and usually causes death. It is possible that the new donor stem cells will begin to grow and then be rejected. This is called graft rejection and then you would be without bone marrow cells. This happens in between 10 to 20 out of 100 patients. With both of these conditions, you will be at greater risk for anemia (low red blood cell count), bleeding (from not enough platelets), infection (from not enough white cells), and possibly death. If graft failure or rejection occurs, you may require additional stem cells which will be obtained from the same family donor.

You need to be aware that if you experience graft failure or rejection and need additional stem cells, the donor may decline (refuse) to donate these additional cells or may be unable to undergo an additional stem cell collection procedure. This would mean that you would not be able to receive these additional infusions and would remain at high risk for severe and possibly fatal bleeding and/or infection. This would also mean that your disease may not be helped by this study treatment. If you experience graft failure or rejection, the doctors will discuss possible options with you.

Veno-occlusive disease.

Some stem cell transplant patients develop a complication called veno-occlusive disease or VOD. VOD causes damage to the small veins of the liver and blocks the blood from going through these veins. This causes the liver to grow large and tender and causes the body to retain fluid. VOD makes it more difficult for the liver to function. These liver changes can cause swelling and tenderness of the abdomen, holding fluid, weight gain, and a condition called jaundice which is a yellowing of the skin and eyes.

VOD is often mild and may cause no permanent damage. However, VOD can be severe and can lead to other problems, including liver failure, lung failure, and death. We cannot predict which patients will get VOD. VOD is more likely to happen when the liver is already damaged. There is still a risk of VOD, even if the liver is not damaged. If you experience severe VOD your doctors will discuss the possible treatment options with you.

Reproductive risks.

The risks of this treatment on reproduction (ability to have a baby or father a baby) in the future are unknown. Chemotherapy often causes sterility (inability to have or father children) which can be permanent or temporary. The effects of this treatment on an unborn or nursing child are also unknown. Females must not be pregnant or breast-feeding a baby when starting treatment and must not get pregnant during treatment. Females of childbearing age must have a negative pregnancy test before starting the treatment. If you think you may have become pregnant during the treatment, you must notify your doctor immediately. If you become pregnant, the treatment may be stopped.

There may be risks associated with male patients fathering a child while receiving this transplant treatment. Some medications cause DNA damage. This may be passed on to children through sperm, resulting in possible birth defects or babies with abnormalities.

Patients who are able to have a child or father a child must use an effective form of birth control while receiving this treatment. Effective forms of birth control include oral contraceptive pills, condoms, and abstinence (not having sexual intercourse). Birth control methods should be continued for at least 6 months after treatment to avoid pregnancy. We also do not know if there may be unknown long-term effects your future children.

Chemotherapy and other agent related risks:

Common side effects of chemotherapy include nausea, vomiting, hair loss, mouth sores, stomach ulcers, and low blood counts. Low blood counts can mean that you are at a higher risk for infection (which may require antibiotic and hospitalizations), bleeding, and anemia (weakness and pale skin). This may require blood and/or platelet transfusions. Allergic reactions may occur with any medicine.

A possible late side effect of this study treatment and related medications is therapy-related cancer. The exact risk is not known but is thought to be less than 1% in the first 20 years of follow-up.

The following pages describe possible side effects specific to each of the study related agents that you will receive as part of this research study. However, unknown side effects may occur.

The symbol # before any side effect means that this problem is rare (# = rare).

RADIATION THERAPY (Total Lymphoid Irradiation or TLI)

- Redness and/or brown staining of the skin
- Upset stomach and vomiting
- Low blood counts
- Stunted growth
- Hair loss
- Sterility (inability to have children)
- Lung damage
- Heart disease
- Thyroid gland disease
- Cancer or second cancers

CYCLOPHOSPHAMIDE (Cytoxan®)

- Nausea and vomiting
- Hair loss
- Low blood counts with higher risk for infection, bleeding, and anemia
- Bladder problems that cause pain when urinating or cause blood in the urine. (May be prevented by giving extra amounts of fluid by mouth or by vein, or by a drug called MESNA.)
- Sterility (unable to have children)

Second cancers (very rare)
Lung damage (pulmonary fibrosis)
Blurred vision
Abnormal heart beats (at high doses)
Heart damage
Mouth sores
Problems with body fluids and electrolytes (SIADH)

FLUDARABINE (Fludara®)

- Low blood counts with higher risk for infection, bleeding and anemia
- Mild nausea and vomiting
- Loss of appetite
- Tiredness, feeling bad, weakness, fever, chills
- Nerve pain, decreased feeling in hands and feet (21-60 days after therapy), eye problems, and hearing problems
- Cough or difficulty breathing
- Nerve damage with high doses

Redness, swelling or sores in the mouth or throat

MELPHALAN (Alkeran®)

- Nausea and/or vomiting and/or diarrhea
- Hair loss
- Low blood counts with higher risk for infection, bleeding, and anemia
- Allergic reactions (skin rash, redness, itching) swelling

- Sterility (unable to have children)
- Anaphylaxis (severe allergic reaction) with low blood pressure, rapid heartbeat, sweating and shortness of breath
- Skin sores or ulcers if the medication leaks out of the vein
- Mouth sores

Second cancers
Lung damage (pulmonary fibrosis)
Liver damage
Permanent failure of the bone marrow (very rare)

MESNA (Mesnex®)

Stomach pain
Diarrhea and/or loose stools
Headache
Limb and joint pain
Tiredness
Allergic reactions
Low blood pressure

THIOTEPA (Thioplex® by Immunex) (TESPA, TSPA)

- Low blood counts, with higher risk for infection, bleeding, and anemia
- Pain at injection site
- Nausea and vomiting
- Loss of appetite, weight loss
- Mouth sores
- Headache, dizziness
- Changes in menstrual cycle for females

Impaired fertility for males (inability to father a child)
Changes in skin color
Allergic reactions, including skin rash and hives
Breathing problems, lung damage
Bleeding from bladder or kidney failure, kidney damage
Second cancers like leukemia

MYCOPHENOLATE MOFETIL (MMF, CellCept®) *(if needed)*

- Low blood counts with increase chance of infection, fever or bleeding
- High or low blood pressure
- Difficulty sleeping (insomnia)
- Headache
- Dizziness
- Rash
- Acne
- Swelling of hands, feet or ankles (peripheral edema)

- Tremors
- Anxiety
- Tingling or burning feeling in the skin
- Nausea or vomiting
- Decreased appetite
- Diarrhea or constipation
- Stomach pain or cramping
- High cholesterol
- High or low potassium in the blood
- Low phosphorous in the blood
- High blood sugar
- More frequent urination
- Burning with urination
- Blood in urine
- Kidney damage
- Shortness of breath
- Cough or sore throat

Bone or muscle pain or cramping
Bleeding of the stomach or intestines
Eye problems
Increased chances of some tumors or cancers

What are the benefits of the study?

We do not know if you will benefit from being treated with this study transplant procedure. It is possible that this study treatment may help to put your disease in remission or keep it in remission. However, there is no guarantee that this will work. You may benefit from knowing that the information learned from this study may be able to help future patients with a cancer such as yours that may be difficult to treat.

Payments for your time spent taking part in this study

You will not be paid to take part in this study

What about new information?

You will be told of any new information learned during the course of the study participation, which might cause you to change your mind about continuing this treatment. If you are interested in learning more about this treatment, you may contact Dr. Brandon Triplett at 901/595-3300.

How will I find out the results of this study?

The researcher will give you information about the overall results of this study. Whether you will know your personal test results will be discussed in another part of this document. St. Jude researchers share information with people in studies in many ways, including:

- Articles on www.stjude.org

- In newsletters
- In medical or scientific journals
- In the media

Published research results will only describe groups of people who took part in the study. Information that points out a single person will not be in research journals or other reports.

What about privacy?

Your medical records will be kept private to the degree allowed by law. Information from your medical records will not be given to anyone outside the hospital other than that specified in this document unless you agree.

Government agencies such as the FDA oversee medical treatment of people as required by state or federal regulations. Therefore, it may be necessary for these government agencies to review parts of your medical record.

Information about you may also be shared with representatives from the Miltenyi Biotec Corporation, the manufacturer of the investigational CliniMACS stem cell selection device. This information will include but is not limited to the donor cell product data, conditioning medications used, infusion date, side effects and information about how your immune system and disease have responded to the transplant procedure. Representatives from Miltenyi Biotec may review your laboratory and medical records to verify protocol and stem cell processing compliance**.**

The Transplant Program at St. Jude Children's Research Hospital is required by the United States federal government to report all transplant and post-transplant follow up information to the Center for International Blood and Marrow Transplant Research (CIBMTR). The CIBMTR is worldwide research organization of scientists and doctors who study important issues in transplantation.

Your stem cell collection related information will also be sent to and reviewed by representatives from the Foundation for the Accreditation of Cellular Therapies (FACT). FACT is an international oversight group responsible monitoring the clinical and laboratory activities of institutions that provide research and treatment with certain blood cell products including stem cells. These representatives may review your laboratory and medical records to verify institutional compliance with federal regulations regarding these blood cell products.

Data sent to the CIBMTR and FACT will not include your St. Jude record number. A unique identification number will be assigned to your information. However, some of the information sent may possibly be linked to you. This information includes but is not limited to the following:

- Your date of birth and primary country (and state) of residence;
- Type of cancer, prior cancer related therapy, dates of and results for all immune system and infectious disease related blood tests;
- Medications, doses used during study treatment, infusion date, side effects of the treatment;

- How your immune system, blood system and disease have responded to the study treatment.

It is important that you are aware that, because this information may be linked to you, absolute privacy cannot be guaranteed.

By signing this consent form, you are allowing your data to be sent to and medical records to be reviewed by these persons.

- Government agencies such as the FDA and the National Cancer Institute (NCI).
- Miltenyi Biotec, the maker of the investigational CliniMACS device.
- A regulatory agency called FACT.
- A research organization called the CIBMTR.
- A research safety and ethics review committee, called the St. Jude Institutional Review Board (IRB).
- The St. Jude Institutional Biosafety Committee (IBC). An internal committee that oversees all aspects of investigational biologic products (which includes blood cell products processed through the use of an investigational device such as the CliniMACS), as well as all laboratory and clinical related safety issues.

SUMMARY OF RESEARCH AND PRIVACY RIGHTS

Therapeutic Research

The following statement describes your rights as a research participant in this study:

1) You may refuse to be in this research study or stop at any time. This decision will not affect your care or your relationship with your doctor or St. Jude. If available, you may receive routine medical care at St. Jude Children's Research Hospital.

2) If you have insurance, TennCare or Medicaid, or other health care coverage such as an employer-sponsored benefit plan, they will be billed for many of the services we provide. However, we do not bill patients or their families for the cost of medical care not covered by their health plans. This includes research costs.

3) Your samples and information may be used to develop a new product or medical test, which may be sold. If this happens, you will not receive any payments for these new products.

4) If you have any questions about this study or if you are injured as a result of this study, contact Dr. Brandon Triplett**,** at 901-595-3300 immediately. If you are injured from being in this research study, St. Jude will provide reasonable and necessary care for that injury. If you need more care than St. Jude can provide, we will help you find medical care somewhere else. It is not the hospital's policy to provide payment if you are injured from being in this study; however, you are not giving up any of your rights by signing this consent form.

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

6) A decision to take part in this research means that you agree to let the research team use and share your health information also called protected health information (PHI) for the study explained above. This information will be kept indefinitely. You have the right to see, copy, and ask for changes to your protected health information that will be used or given out. However, research information may not be seen until the end of the study.

7) When you first registered at St. Jude, you received a copy of the St. Jude Notice of Privacy Practices. It tells how your PHI may be used or given to someone outside the hospital. You have the right to read the Notice of Privacy Practices before you sign this form. It may have changed since you first registered at St. Jude. You can find it at the bottom of every page on the St. Jude Internet website: *www.stjude.org*.

8) Federal agencies such as the Food and Drug Administration (FDA), the Office of Human Research Protections (OHRP) or the National Institutes of Health (NIH), St. Jude Children's Research Hospital Institutional Review Board (IRB), your insurance company or other health benefits plans (if charges are billed to these plans), as well as other regulatory agencies, committees, or persons involved in overseeing research studies may review your research and medical record.

9) Information about you that may be given out includes your complete medical records, including details about diagnosis, illness, treatment, and information that may be recorded about past diagnosis or treatment and information taken as a part of this research study as explained in this informed consent.

10) After your records are given to or used by others, St. Jude Children's Research Hospital cannot promise that information will not be given out again. Also, the information given out may no longer be protected by federal privacy laws.

11) St. Jude uses reasonable safeguards and means to protect your private information. However, St. Jude cannot guarantee the security and confidentiality of e-mail, text messages, fax communications or mail.

12) Researchers and study staff are required by law to report suspected child abuse, threat of harm to self or others, and certain diseases that spread from person to person.

13) Your permission to use and give out your child's protected health information will end when your child turns 18 years of age. At that time, we may contact your child for his or her permission to continue using it.

14) You may take back permission for your records to be used or given out at any time, for any reason, except when that information has already been given out or used for the study based on your permission. To take back your permission, please fill out a form called a Revocation of Release of Authorization. You may ask for this form by calling the St. Jude Privacy Officer at 901-595-6141. You must mail the form or hand it to:

    HIPAA Privacy Officer
    St. Jude Children's Research Hospital
    262 Danny Thomas Place, Mail Stop 280
    Memphis, TN 38105

15) You can get more details about your rights as a research participant by calling the St. Jude Institutional Review Board at 901-595-4357 or the Research Participant Advocate at 901-595-4644. If you are outside of the Memphis area, please call toll-free 1-866-583-3472 (1-866-JUDE IRB).

16) The St. Jude Research Participant Advocate is an individual who is not part of the research study team and is available to you to discuss problems, concerns, and questions. The Advocate can help you obtain information and can relay any input you may have concerning the research to the research study team. You can reach the Advocate by calling 901-595-4644, or if you are outside of the Memphis area, call toll free at 1-866-583-3472 (1-866-JUDE-IRB)

17) You will be given a copy of this signed consent form.

PARENT/GUARDIAN STATEMENT (Required for patients younger than 18 years):

I have read this document or it was read to me. I have been encouraged to ask questions and all my questions have been answered. I give permission for my child to be in this research study.

_____	_____	_____ AM/PM
Parent/Legal Guardian Signature	Date	Time (circle one)

ASSENT DISCUSSION (Required for participants 7–13 years old)

☐ The research was explained to the minor participant in age-appropriate terms and the minor verbally agreed to take part in the study.

☐ Minor declined to take part in the study. The minor declined for the following reason(s): _____

☐ An assent discussion was not initiated with the minor for the following reason(s):

- ☐ Minor is under 7 years of age.
- ☐ Minor is incapacitated.
- ☐ Minor refused to take part in the discussion.
- ☐ Other _____

RESEARCH PARTICIPANT'S STATEMENT (14–17 years old and Adult Participants 18 years old or older):

I have read this document or it was read to me. I have been encouraged to ask questions and all my questions were answered. I agree to take part in this research study.

_____	_____	_____ AM/PM
Research Participant Signature	Date	Time (circle one)

RESEARCHER/DESIGNEE STATEMENT:

I have explained the research to the participant and his/her parent(s) or legal guardian(s). The research participant and parent(s)/guardian(s) were encouraged to ask questions and all questions were answered to their satisfaction. A copy of this form has been given to the participant or his/her representative.

_____	_____	_____ AM/PM
Researcher/Designee Signature	Date	Time (circle one)

_____
Print Name

RESEARCH PARTICIPANT ADVOCATE STATEMENT:

I observed the informed consent process. The research study, intervention/observation, risks, benefits, and alternatives were presented to the research participant and/or legal guardian(s). They were encouraged to ask questions, and research team members answered all their questions. The participant/parent(s) indicated that they: 1) understood the information presented; and 2) voluntarily consented /agreed to take part in the research.

_____	_____	_____ AM/PM
Research Participant Advocate	Date	Time (circle one)
_____	_____	_____ AM/PM
Interpreter (if needed)	Date	Time (circle one)

PLEASE FAX CONSENT FORM TO PROTOCOL OFFICE #6265