Official Study Title: TCRαβ-DEPLETED PROGENITOR CELL GRAFT WITH ADDITIONAL MEMORY T-CELL DLI, PLUS SELECTED USE OF BLINATUMOMAB, IN NAIVE T-CELL DEPLETED HAPLOIDENTICAL DONOR HEMATOPOIETC CELL TRANSPLANTATION FOR HEMATOLOGIC MALIGNANCIES

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Note: When we say "you" in this informed consent document, we mean "you or your child." When we talk about research, it can be called a clinical trial, research study (study), or research protocol.

Key Information

To start, we highlight here the risks, benefits and study requirements that we think you should know before deciding if you want to take part in this research study. If you're still interested, we'll then get into more details.

A. Why are you being asked to voluntarily take part in this study?
   You are being asked to take part in this clinical trial, a type of research study, because you have a family member, with cancer, who will receive a hematopoietic (blood) cell transplant at St. Jude Children's Research Hospital
B. What is the usual approach to providing a blood cell product to a transplant recipient?
   Treatment for your family member's cancer includes blood cell transplantation. The procedures used to collect blood cells from you while in this study, are the same procedures that would be used to collect blood cells from any other donor. These procedures are called mobilization (increases number of cells in the blood) and apheresis (actual collection of the cells).
C. Why is this study being done?
   The purpose of this study is to learn more about newer methods of transplanting blood cells donated by a family member to children with high risk cancers of the blood or lymphatic system. This includes the effects of the chemotherapy, the transplant cell product, and the additional white blood cell (lymphocyte) infusion on the transplant recipient's body, disease and overall survival.
D. What will happen if you decide to take part in this study?
   First you will complete a screening process to ensure that you are healthy enough to be a blood cell donor. This includes collecting a medical history, blood tests and performing a physical exam. If you agree to the optional blood testing, we will collect these samples prior to the collection of your blood cells. The two collection procedures will take place in the St. Jude Blood Donor Center and will take 1 to 2 days each. For the second collection, you will be required to undergo a mobilization procedure. This includes receiving the medication G-CSF, an injection under your skin, which will take place in the St. Jude Medicine Room. You should not have to be admitted to the hospital overnight for any of these procedures, all will be completed as an outpatient.
E. What are the research risks and benefits of taking part in this study?
   The most common risks to serving as a blood cell donor:

a. Side effects from the medication, G-CSF (Filgrastim). This medication can make you feel sick, like you have the flu. You may also have joint and bone pain. These side effects are usually mild and last for only a short time.

b. Side effects from apheresis. You can experience pain from the insertion of the needles used to collect the blood cells, and you may be at risk of infection at the site where the needles are placed.

c. In addition, you must not undergo either one of the donor procedures, mobilization or apheresis, if you are pregnant.

F. How many people will take part in this study?
We expect that up to 30 transplant recipients will take part in this study over the next few years, therefore we also expect 30 donors to take part.

G. What are your options?
1) Taking part in this research study is completely your choice.
2) If you decide to take part in this study, you can change your mind and stop at any time.
3) If you leave the study, you may place the transplant recipient at a high risk for severe and possibly fatal bleeding and/or infection.
4) You may choose not to be a donor on this study.

If you are still interested in taking part in this research study, HAP2HCT, more detail is provided below in the following pages.

Study Contact Details and Further Information

You are encouraged to ask any questions you wish, before, during or after your treatment. If you have any questions about the study, please speak to your doctor, who will be able to provide you with the up-to-date information about the drug(s)/procedure(s) involved. If there is anything that you do not understand, or if you have any other questions, please contact any of the people below.

Who to talk to for…	You can contact…	At…
• Any new or unexpected symptoms, side effects or discomforts • General study questions • Research related injuries • Any research concerns or complaints • Any medical or surgical treatments done outside of St. Jude such as with your local doctor or another hospital during this study	**Principal Investigator, Researcher** **Dr. Brandon Triplett** 262 Danny Thomas Place Memphis, TN 38105	901-595-3300 (Main Hospital Number)
• Your rights as a research participant • Any research concerns or complaints	**Institutional Review Board (IRB)/Research Participant Advocate** * IRB is a group of scientists and community members who make sure research meets legal and ethical standards * Research Participant Advocates are individuals who are not part of the research study team and are 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 and the IRB.	901-595-4644 or 901-595-1139

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1. Why are you being asked to voluntarily take part in this research study?

You are being asked to take part in this study as a hematopoietic progenitor (blood making) cell donor for a family member who will receive a hematopoietic (blood) cell transplant at St. Jude Children's Research Hospital. . Taking part in this study is completely your choice. Please take your time in deciding and feel free to discuss it with your family, friends, and St. Jude staff. Before agreeing, it is important that you read this informed consent document (consent form) that describes the study. After you understand the study and if you agree to take part, you will be asked to sign this consent form. You will be given a copy to keep.

2. Who is sponsoring this study?

This study is being sponsored by St. Jude Children's Research Hospital. The principal investigator (researcher) in charge of this study is Dr. Brandon Triplett, who can be reached by phone at 901-595-3300, if you have any questions or concerns about this research.

3. What is the purpose of this study?

The purpose of the study is to learn more about the effects (good and bad) of transplanting blood cells donated by a family member that have been modified in a laboratory, to children and young adults with a high risk cancer that is in remission but is at high risk of relapse. This study is different from previous studies in that a different type of hematopoietic blood cells (TCRαβ-depleted) will be collected to be given to the recipient. The TCR (T-cell receptor) is a molecule that is found only on T-cells. These T-cell receptors are made up of two proteins that are linked together. About 95% of all T-cells have a TCR that is composed of an alpha protein linked to a beta protein. This blood cell infusion will be followed by an additional infusion of donor memory cells called lymphocytes (CD45RA-depleted and CD19+ depleted). This study will be testing the safety and effects of the chemotherapy and the blood cell infusions on the transplant recipient's disease and overall survival.

4. What will be done in this study?

Summaries describing each of these steps are noted below. Your doctor also will provide additional details and answer any questions you may have. This study apheresis procedure includes the following:

- Donor screening
- Research test (optional blood immune tests described in section 17)
- Lymphocyte collection (may also be performed at a later point if needed)
- Blood progenitor cell mobilization.
- Blood progenitor cell collection
- Additional mobilization and collection (if needed).

Donor screening

After signing the consent form, you will be asked to complete some further screening tests or procedures to find out if you can continue to take part in this research study. These tests and procedures are the same as those that are required for all persons who would be providing a blood product to be given to another person. If you have had some of these tests and procedures done recently, they may or may not need to be done again. Screening includes:

- Medical history (health status, immunizations, current medications, any exposure to infections)
  - Physical exam to determine if you are healthy to proceed with donation
  - Blood tests to look for bacteria and viruses (including but not limited to: cytomegalovirus (CMV), hepatitis B and C virus, human immunodeficiency virus (HIV), human T-cell lymphotropic virus (HTLV-I/II), syphilis, and West Nile virus (WNV); (about 1 tablespoon of blood or 3 teaspoons or 15 mL)

    It is possible that your donated blood cells can be used for your family member's study transplant procedure even if your blood tests and screening show that you may currently have a communicable disease or are at high risk for passing a disease or infection onto others.
  - Blood and urine samples for routine laboratory tests (blood counts, chemistries, coagulation, and urinalysis) to see how well your body systems such as the bone marrow, liver, kidney, heart, etc. are working; (about 1 tablespoon of blood or 3 teaspoons or 15 mL)

You have the right to learn the results of your health screening including infectious disease tests. Your doctor will notify you of any abnormal results. Additional studies and doctor's visits may be needed to further evaluate any abnormal results. If any of the results do not allow you be a donor, your doctor may suggest or send you to other doctors for additional evaluation, testing and treatment, if needed. These costs may not be covered by St. Jude Children's Research Hospital and may be the responsibility of you or your insurance company.

Research tests

There are optional blood immune tests that the study team would like to perform that will be discussed in section 17 of this consent.

Lymphocyte collection

You will be donating for two different blood cell products for the recipient. This first product will contain mature immune cells that will be used to strengthen the developing immune system in the recipient, this is known as a donor lymphocyte infusion (DLI). The procedure used for collecting these cells from the blood is called apheresis.

Apheresis is a process that uses a machine to draw blood from a vein in one arm and pass it through a machine that separates the blood into parts (plasma, platelets, white blood cells, and red blood cells). One or more of these parts will be removed from the blood. The remaining parts will then be mixed together and returned to you through a vein in your other arm. The parts of your blood that were removed will be processed and given to your family member as part of their treatment.

Apheresis for the lymphocyte product will typically occur prior to starting the mobilization procedure for the progenitor cell product; however, it may occur following the mobilization procedure as long as 14 days have passed.

Blood progenitor cell mobilization

The second collection of blood cells will be used for your family member's blood progenitor cell transplant. Blood progenitor cells are immature (young) cells that usually live in the bone marrow. These cells can become any type of blood cell - a white cell to fight infection, a red cell to carry oxygen, or a platelet to clot the blood. To get these cells to leave the bone marrow and travel temporarily in the blood for collection, we use a procedure called mobilization.

This mobilization is to increase the number of progenitor cells in your blood so that more cells can be collected for your family member's transplant. For this you will receive a blood growth factor called "granulocyte colony stimulating factor (G-CSF or Neupogen) over five to six days, once or twice daily until enough progenitor cells are available in your blood. Growth factors are proteins similar to hormones naturally produced in the body. G-CSF is usually given as a shot under the skin. This drug will help your body to increase the number of progenitor cells in your circulating blood by moving ("mobilizing") or pushing these cells out of the bone marrow into the bloodstream.

The schedule and doses of G-CSF may change depending on how many progenitor cells your body is able to make during the mobilization. A blood test will be done which will tell your doctors how many are in your blood stream. If enough are there, you will go on to the next step in the blood cell collection process called apheresis. If there are not enough progenitor cells in your blood stream, then you may receive one or two additional days of G-CSF. Below is a diagram that gives an overview of the mobilization.

SCHEDULE	GROWTH FACTOR	APHERESIS
Day -5	G-CSF	
Day -4	G-CSF	
Day -3	G-CSF	
Day -2	G-CSF	
Day -1	G-CSF	Apheresis for donor cells
Day 0	G-CSF (if needed)	Apheresis for donor cells (if needed)

Day 0 is the day of the recipient's transplant. The (-) means days BEFORE, and the (+) means days AFTER the recipient's transplant.

Blood progenitor cell collection

These progenitor cells will also be collected using the apheresis procedure described earlier. We expect that you will need to undergo 1 day of blood cell collection using apheresis. It is possible that you may not be able to provide all the needed progenitor cells in one day of collection, meaning that you would need an additional one or two days to collect enough progenitor cells. Needing more than two days of collection is rare.

Sometimes the veins in the arms are not large enough for the apheresis needles. You may temporarily (for a short time) need a special catheter (a small, flexible tube) called a central venous line. However, this rarely occurs. This catheter may be placed in one of the veins in or near your neck or your groin and will be removed when enough progenitor cells have been collected. If you need a central venous line, you will sign a separate consent form for the procedure.

During apheresis, you will receive drugs to keep your blood from clotting (anti-coagulants) in the machine. These drugs are called citrate and heparin and may be given either alone or together. Apheresis takes between three to eight hours per day and will continue until enough cells are collected. During the donation procedure, you will need to lie fairly still in a recliner chair. You can sleep, watch TV, or watch a movie. One or two family members or friends may visit with you during the procedure. You may have drinks or snacks brought to you.

The apheresis procedure will not deplete (use up) the blood or marrow cells in your body. Healthy people, especially healthy adults, have a large amount of these cells in their body and are able to replace their donated cells with new ones soon after donation (about 1 to 2 weeks). Apheresis for the progenitor cell product will occur on the day before the recipient's scheduled transplant and then it may occur again the day of the transplant.

After your cells are collected, they will be processed and filtered in a laboratory at St. Jude using a machine called the CliniMACS™ device. This process will be done on both the progenitor cell product and the lymphocyte product. The CliniMACS™ device has been approved for use in the United States by the Food and Drug Administration (FDA). However, the CliniMACS™ process that we will use on your cells in this study has not been approved. That means that the processing of your blood cells

using this device is considered experimental. After your blood cells are processed, they will be infused (transplanted) into your family member through his/her veins.

Additional mobilization and collection (if needed)

Your family member will be monitored frequently for the number of donor cells (your cells) found in his/her blood. This number should increase as the progenitor cells begin to grow in the bone marrow. However, he or she may have a decrease in the number of these donor cells found in the blood. If this happens, we may need to give additional lymphocyte products. These lymphocytes can be collected by apheresis as before, or they may be collected as a standard whole blood donation (blood is donated, not filtered nor returned to you).

We will ask you to remain on this study until it is determined by your family member's doctor that no further cell infusions are needed. This could be as long as your family member is taking part in the study, which is one year.

5. What are the risks and benefits of taking part in this study?

a. Risks

The mobilization and apheresis are generally well tolerated although most donors do have some mild to moderate side effects.

Side Effects of G-CSF. The side effects of G-CSF usually are mild and short-lived, and may include low grade fever, mild nausea and vomiting, abdominal cramping, diarrhea, headache, bone and joint pain, muscle aches, tiredness, trouble sleeping, rash, and worsening of skin conditions such as psoriasis or eczema. G-CSF can cause an increase in the white blood cells, and a decrease in the platelet counts. Rarely, allergic reactions which include wheezing, shortness of breath, fast heart rate, itching, dizziness, and/or low blood pressure may occur. More serious reactions such as heart attack, splenic rupture (bleeding into the belly) or blood clots have been noted. While some of these side effects may be life-threatening, this is a very rare possibility.

G-CSF is usually given as a shot under the skin, which may be painful or cause bruising. Serious problems are very unlikely to occur and most symptoms go away within 2 to 3 days after stopping G-CSF. Bone, joint pain, and muscle aches may occur. The bone pain is usually relieved by over-the-counter medications which your doctor will discuss with you. However, the pain may be severe enough to require stronger pain medication. Prolonged (extended time) soreness and pain may disrupt your normal daily activities. Some donors return to their normal activities in a day or two, while others may need a week or more due to soreness and bone pain.

If you experience any soreness or pain, please notify your doctor immediately. Your doctor can suggest or prescribe medication or treatment to help lessen or relieve your pain and discomfort.

Long-term safety data on G-CSF when administered to healthy people is limited; however, to date no long-term side effects of the medication have been seen.

Side Effects of Apheresis. The apheresis procedure has side effects like the side effects that can happen when people donate whole blood. These side effects include pain, discomfort and/or infection at the sites where the needles are placed. Also nausea, fainting or dizziness, and/or blood loss may occur. If the procedure is stopped before it has been completed, it is possible that a part of the blood taken out will not be returned to your body.

After apheresis, your platelet count and white blood cell count will likely be lower than before the procedure. Some donors will have platelet counts that are mildly low, while others may have severely low platelet counts. The likelihood of you having a severely low platelet count is low. However, low platelet counts (mild or severe) may increase your risk of bleeding. Having a low platelet count (mild or severe) is temporary. You may need a transfusion of red blood cells or platelets; however this rarely happens. Taking aspirin in combination with a lowered platelet count may increase the chance of bleeding. Therefore, aspirin, medications that contain aspirin or medications that contain ibuprofen (i.e. Motrin®) must not be taken while getting G-CSF or for 2 weeks after blood cell donation without permission from your doctor.

*Side effects of citrate and heparin***.** If citrate is used during apheresis, you may have muscle cramping, numbness, a cold feeling, tingling sensations, or feel anxious. In rare cases, citrate can cause seizures. If heparin is used, it may take longer than normal for the blood to clot after the apheresis. This longer clotting time may lead to bleeding in very rare cases.

Side effects of the intravenous (IV) catheter used for apheresis procedure. The side effects of the intravenous catheter include fainting, discomfort and bruising at the site where the catheter is placed. Bleeding or infection may occur at the site, however, this is unlikely.

Side effects of obtaining blood for blood tests. The side effects of obtaining blood samples include fainting, discomfort and bruising at the site where the needle was placed. Bleeding or infection may occur at the site, however, this is rare.

Psychological risks of donation. Your family member may have side effects (good and bad) as a result of the infusion of your blood cells. The bad side effects can be mild or moderate but may also be life threatening or fatal (cause death). If your family member were to have a bad side effect, you may become sad or depressed. You may feel anxious or have feelings of guilt. If this occurs, please talk to your doctor. Your doctor will discuss these feelings with you and, if needed, help you obtain proper counseling or treatment.

Loss of confidentiality. Very rarely, personal information from your records could be given out by accident. This might make you upset, embarrass you, or affect your ability to get insurance. To stop this from happening, we:

- Store records apart from names or other personal information
- Only allow members of the study team to see the records
- Store electronic data only on computers protected with a password and encryption software
- Report study results on the whole group and never identify one single person in any reports

There is an additional risk related to confidentiality and results from your screening tests concerning infections. If your doctor finds that you have or may have an important medical condition that may impact the safety of the recipient if given your blood cells, this information will have to be made known to the recipient and his/her legal guardian(s) (if under 18 years old) before you can start the donation procedure. This means that the transplant recipient/legal guardian(s) will be told of any medically significant disorders that you may have before you can donate. This is so that they can make an informed choice as to receive or not receive your donated blood cell product.

If your blood tests show you have a communicable disease, your donated blood cell product, identified by your St. Jude medical record number (not your name) would need to note the following: "WARNING: Reactive test result for (name of disease agent or disease)" and "WARNING: Advise patient of communicable disease risk."

If your screening questionnaire indicates that you have been or may have been exposed to a communicable infection/disease, then the label must note - "WARNING: Advise patient of communicable disease risk." Therefore, for the purpose of assuring medical safety of the transplant recipient, absolute confidentiality of the results of your screening process cannot be guaranteed. If you do not agree for this information to be disclosed to the recipient/legal guardian(s), then you cannot donate and take part in this study.

Other side effects. It is possible that this research study also involves risks that we currently do not know about. If you experience any side effects or discomfort during mobilization or apheresis, tell a nurse or a doctor immediately.

There are no risks to you related to the processing of your blood cells using the investigational CliniMACS device. This is because the processing is done after the cells have been taken out of your body.

> As the donor, you will receive no direct benefit from donating blood cells. However, you may receive some psychological benefit knowing that your donated cells may help to lessen your family member's disease. Your donation may also help doctors gain information related to the study treatment and may help other children in the future with cancer who undergo this type of transplant procedure.

The risks of the required genetic/genomic testing are explained below in the Genetic/Genomic section.

b. Benefits

As the donor, you will receive no direct benefit from donating blood cells. However, you may receive some psychological benefit knowing that your donated cells may help to lessen your family member's disease. Your donation may also help doctors gain information related to the study treatment and may help other children in the future with cancer who undergo this type of transplant procedure.

6. What are the risks to pregnancy, to an unborn child, and to the ability to have children (fertility) when taking part in this study?

Some treatments, including (but not limited to) G-CSF mobilization and apheresis can include risks to pregnancy and an unborn child. These risks can be short-term or permanent. These risks and birth control options are discussed below for both males and females. Please discuss any concerns you may have about future fertility with your doctor. Treatments on this study may involve risks to the pregnancy, the unborn child, or fertility that we currently do not know.

Donors must use an effective form of birth control while undergoing mobilization and the apheresis procedure. Effective birth control methods include oral contraceptive pills, condoms and abstinence (not having sexual intercourse). Birth control methods should then be continued for at least two weeks after the completion of the mobilization and apheresis procedure to avoid pregnancy.

Male Risks:

There may be risks associated with fathering a child while undergoing mobilization.

Female Risks:

You must not take G-CSF or undergo apheresis if you are pregnant. The medications could cause a birth defect in an unborn child. Females will be required to take a pregnancy test before starting mobilization. If you are pregnant, you cannot take part and serve as a donor. If you become pregnant at any time during participation, you must notify the study doctors immediately. If this occurs you will be taken out of the study and unable to provide any additional progenitor cells for your family member

Fertility (ability to have children) Risks:

We also do not know if there may be unknown long-term effects of the mobilization treatment and apheresis procedure to your future unborn children.

7. Can you stop taking part in this study?

a. Can you change your mind about participating in this research study?

You can change your mind about taking part in this research study and stop at any time. However, if you decide to stop the procedure, you need to talk to your doctor first. If you leave the study you may place the transplant recipient at a high risk for severe and possibly fatal bleeding and/or infection. Your doctor will discuss this further with you.

If you change your mind about participating in this study, samples or related information that have already been used by researchers will not be returned or removed.

b. Can you be taken out of this study without your consent?

The procedure may be stopped and you may be taken out of the study without your consent for the following reasons:

- You need a treatment not allowed while undergoing mobilization and/or apheresis.
- You develop a change in your health status, including a risk for/development of communicable disease, which in the opinion of your doctor would make blood cell collection or continued study participation not in your best interest or that of your family member (the recipient).
- You are unable to keep appointments or take the growth factors as required for mobilization.
- You have a positive pregnancy test.
- New information is learned that a better way of collecting blood progenitor cells is available, or that study participation would be harmful or not in your best interest.

8. What are you other options and can you have other treatments while taking part in this study?

a. Other Treatment Options

You are not required to be a donor or to have your blood cells collected by mobilization and apheresis. An alternative option to blood cell donation is to not be a donor.

Your doctor and clinic staff taking care of you will be available to answer any questions about this collection process and the other options available, either now or in the future.

b. Can you participate in other research studies at the same time?

Please check with your study doctor before thinking about taking part in any other research.

c. Other medications, vitamins, and supplements

While in this study, you may not be able to take some or all of the medications or treatments you may be taking. It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture, or other alternative treatments.

Tell your study doctor about any changes to these during your participation in the research study. Your study doctor will explain to you which treatments or medications need to be stopped for the time you are involved in the research study.

$ 9. How much will it cost you to take part in this study?

If you have health care coverage, we will bill your health care insurer for all standard of care services, tests, and procedures, as applicable. Billing your health care insurer impacts your annual deductible and life-time maximum, if any. This may affect your health care coverage to some extent if you go to another health care provider or institution in the future.

At St. Jude, you will not be responsible for or receive bills for co-pays, co-insurance, deductibles, or similar patient-liability amounts, or for the cost of medical care related to your disease or this study not covered by your health insurer. This includes research-only costs. Research-only tests and procedures (such as optional biopsy or blood samples for biomarker testing) will not be billed to you or your health care insurer.

10. Will you be paid for your time or expenses while taking part in this study?

You will not be paid for your time or expenses to take part in this study. Also, your samples and/or 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.

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11. What if there is a problem while taking part in this study?

If you have any questions about this study or if you are injured from being in this research study, please notify your St. Jude Doctor or the study doctor, Dr. Brandon Triplett, at 901-595-3300 immediately. St. Jude will offer you reasonable and necessary medical treatment for that injury. If you need more care than St. Jude can provide or if you prefer to seek treatment elsewhere, we will help you find medical care somewhere else. St. Jude may bill your insurance company or other third parties, if appropriate.

It is not the hospital's policy to provide payment for other types of costs, such as lost wages, disability, or discomfort if you are injured from being in this study. You are not giving up any of your rights by signing this consent form.

12. How will new findings related to your participation in this study be shared with you?

You will be told of any new information learned during the course of the study which might cause you to change your mind about continuing to take part. You have the right to learn about the results of the study. If you are interested in learning more about when and how to get the results of this research study, you may contact Dr. Brandon Triplett at 901-595-3300.

13. How will you find out the results of this study?

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
- A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by the 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.

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.

14. Will any genetic tests be done and what are the risks of genetic testing?

We will obtain immune cells during this study. Research blood draws will include some genetic testing. Genetic testing on material obtained from these samples should help us learn how your immune cells work, and ways to improve therapies in the future.

The genetic tests are optional and considered research only tests. Results are not reported to you or placed in your electronic medical records. The genetic tests include a partial analysis of genetic material obtained from the samples, and may include whole genome sequencing of normal cells from your body. No direct benefits to participants are expected from these genetic tests.

Information obtained from reading through your genes, as well as information about your health condition, will be entered into one or more scientific repositories or databases maintained by St. Jude Children's Research Hospital, the Federal Government, the European Genome-phenome Archive, or others.

Risks of Germline Genetic/Genomic Testing

There may be risks to your privacy and the privacy of your relatives from storing your information in a database. Although measures are taken to protect your privacy, we do not know how likely it is that your identity could become re-connected with your genetic and health information, and confidentiality cannot be guaranteed. If your genetic information were re-identified, personal information about you, your health, and your risk of disease could become known to others and potentially used to discriminate against or stigmatize you, your family, or your groups. This could also present unknown risks. We believe the chance that this will happen is very small, but we cannot make guarantees. Your privacy and the confidentiality of your data are very important to us; we will make every effort to protect them.

There is a chance that the genomic test results of your normal tissue will show that you have an inherited health condition, or a condition that can be passed down to any children you have. The condition discovered might show that you and possibly other family members are at risk of developing tumors or at risk of developing other health problems unrelated to cancer. It is also possible that testing your normal tissue sample will not find any genetic changes that will affect your current management or future health risks. Sometimes, genetic testing can find gene changes that we do not completely understand. This uncertainty may lead to anxiety or confusion.

After learning your results, you might feel anxious, upset or frustrated. Your doctor will discuss these concerns with you and arrange for needed follow-up, such as with the Genetics Service or other support services (social work, spiritual care, or psychology).

Currently, the U.S. law known as the “Genetic Information Nondiscrimination Act” (GINA) prohibits discrimination based on genetic findings in some circumstances:

a. GINA prohibits health care insurers from requesting or requiring genetic information of an individual or an individual’s family members or using genetic information for decisions about health insurance coverage or rates, or to exclude preexisting conditions.
b. In companies of 15 or more employees, GINA prohibits employment and employee-related decisions from being made on the basis of genetic information of an individual or an individual’s family members.

GINA protections do not apply to:

a. the presence of disease or a health disorder,
b. life insurance, long-term care insurance, or disability insurance. These insurance companies consider may this information in making insurance decisions affecting you,
c. both health care plans and employment from companies employing fewer than 15 people, and
d. people in the military.
e. There are other health plans that GINA does not apply. Please ask your study doctor if you have any questions.

15. What about identifiable private information and identifiable biospecimens (blood, tissue, urine, cells, and any type of data and/or samples) obtained from you during the study?

If you choose to take part in this study, your data and/or specimens will be used to answer the research question(s) and to publish the findings of this study. 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. You will not own your research data and/or specimens. If researchers use your data and/or specimens to create a new product or idea, including those that may have commercial value, you will not benefit financially. There is no plan to share any money with you.

St. Jude's researchers and their collaborators will store the data and specimens collected in this study in electronic databases and other locations and will store specimens in the biorepository or other locations. They may use the data and/or specimens collected in this study for future research purposes and may share some of the data or specimens with others without seeking further consent from you. You may not receive results from that future research.

Sharing data and/or specimens is part of research. It may increase what can be learned from this study and future studies. Often data sharing is required as a condition of funding or for publishing study results. It is also needed to allow other researchers to validate study findings and to come up with new ideas.

Your data and/or specimens may be shared with government agencies, research collaborators, and other researchers and organizations conducting research that may not be related to this study. Your data may also be put in government or other databases/repositories as mentioned in the section above.

Future research using your samples and data is likely to include studies that look at genomic and genetic information to understand causes and cures for health conditions. Because science constantly advances, we do not yet know what other future uses of research data and/or specimens may include. There is no time-limit on sharing of information.

This future research may be unrelated to the current study and may include outside researchers and organizations from around the world. These organizations may include for-profit companies conducting medical research. We or others who distribute data or samples may be paid for data or samples, including yours. You will not receive payment if this happens.

St. Jude will do its best to protect and maintain your data and/or specimens in a safe way. One of the ways we protect your data and/or specimens is by limiting the uses of the information and the type of information that is shared, especially your personal information. This may occur through data sharing agreements and review by oversight groups within St Jude. Often the data and specimens may be coded to protect your identity before they are shared, and we will keep the key to the code in a secure way.

If data and/or specimens are used or shared with any information that may be likely to identify you, such as your name, address, or medical record number, further institutional review and approval would be required. In these cases, we will review whether additional consent from you is required.

Generally, if your data and/or specimens are used and shared without any personal identifiers or only with information that is less likely to identify you (such as the date of a procedure), further review and approval is not needed, and you will not be contacted.

Data sharing could change over time and may continue after the study ends.

The use and sharing of your data and/or specimens is required for participation in this research study. The purpose of research is to learn and discover new information to make improvements to patient care and/or treatments. To make these improvements, research results must be shared with others. By agreeing to take part in research studies, you are agreeing for your information or data to be used and shared with others. If you are generally not comfortable with the use and sharing of your data and/or specimens in future research as explained in this consent, you should talk with your doctor before agreeing to take part in this study.

16. What about permission to use your data/information (HIPAA Privacy Rule), privacy and confidentiality?

Permission to Use Your Data/Information- HIPAA Privacy Rule and Privacy

The HIPAA Privacy Rule defines the situations in which PHI (protected health information) may be used or given to someone outside of the hospital to be used or released for research and other purposes. PHI includes information such as your name, MRN, date of birth, or other identifying information, including research information placed in your medical record.

To do this research, St. Jude Children's Research Hospital (St. Jude) will need to collect, use, and share your private health information. St. Jude is required by law to protect your health information. By signing this consent form, you give St. Jude permission to use and/or release (share) your private health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

If you sign this consent form, you give permission to all researchers and their staff involved in the study at St. Jude to use or release (share) your health information that identifies you for the research study described in this document.

The health information that we may use or disclose (release) for this research includes all information in your medical record. For example, this could include results of physical examinations, medical history, lab test results or any certain health information relating to donation of your blood cell product.

If you sign this consent form, you give St. Jude permission to share your information for future research studies about disease or advancing science and for future unspecified research. You also give permission for us to place this information on databases as described below under Privacy and Confidentiality.

By signing, you will also give St. Jude permission to put your research information, including testing, imaging, genomic and genetic information, other information and studies, and other sensitive information in your medical record. Information from research testing will be analyzed in a CLIA-certified (medical) laboratory or a research-only laboratory. By signing, you give St. Jude permission to put your research information obtained from a CLIA-certified laboratory into your medical record. Results from research-only laboratories will not be put into your medical record and will not generally be available to you or your doctor.

Any information placed in the medical record becomes a permanent part of your record, is kept indefinitely, and is not protected by a Certificate of Confidentiality (Certificate of Confidentiality, if included with this study, is described below under Privacy and Confidentiality). It is protected like any other part of your medical record as described in the Notice of Privacy Practices. You have the right to see, copy, and ask for changes to your PHI that will be used or shared. However, research information may not be available until after the end of the study.

When you first registered at St. Jude, you received a copy of the St. Jude Notice of Privacy Practices. It tells how your PHI, including research information placed in your medical record, may be used or given to someone outside of St. Jude. You have the right to read the Notice of Privacy Practices before you sign this consent form. It may have changes 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

Federal agencies such as the Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), the National Institutes of Health (NIH), and St. Jude Children's Research Hospital Institutional Review Board (IRB), your insurance company and other health benefits plan (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.

Information about you may also be shared with representatives from Miltenyi Biotec, the maker of the CliniMACS device. The data sent will not include your name, initials, or St. Jude medical record number. A unique identification number will be assigned to the information. This data may include but is not limited to your relationship to the transplant recipient, your age, immune system type (HLA type), infectious disease testing, as well as the mobilization, apheresis and processing related data. Representatives from Miltenyi Biotec may review your laboratory and medical records to verify protocol and cell processing compliance.

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

The Transplant Program at St. Jude is also required by the United States federal government to report all blood and bone marrow cell related infusion information to the Center for International Blood and Marrow Transplant Research (CIBMTR). The CIBMTR maintains a database registry (a computer warehouse) of transplant related data from all patients treated world-wide. This would include some information related to the donor. Registries help public health professionals better understand transplant and trends or developments in this type of treatment. FACT and an organization called the National Marrow Donor Program are part of the CIBMTR. The information submitted will be used for basic registry/international statistical purposes only. The CIBMTR will not use this information for the purpose of research.

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

- Your relationship to the recipient (parent, sibling, cousin)
- Your age in years
- Your blood and HLA type

If during the initial (first) screening process, you are found to be ineligible and unable to donate blood cells for your family member, no information will be sent to this registry. However, your medical record may still be reviewed by representatives from FACT.

By signing this consent form, you are allowing your data and/or biological sample to be sent to and medical records to be reviewed by the following persons:

- Government agencies such as the FDA, OHRP and the National Cancer Institute (NCI).
- A transplant related oversight agency called FACT.
- An international data registry for transplant related information 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.
- Other committees or people involved in overseeing research studies.
- Miltenyi Biotec, the maker of the CliniMACS device system

The people who may view, request, receive, or use your private health information include St. Jude researchers and their staff, and other doctors, nurses, and staff members. Additionally, St. Jude may share your information with other people or groups of people. These include:

- Transplant related oversight agencies or registries that may receive and process PHI (CIBMTR, FACT and NMDP); and/or
- St. Jude Institutional Review Board and St. Jude Institutional Biosafety Committee

You do not have to sign this consent form which gives your permission, but if you do not, you may not receive research-related treatment.

Please note that you may change your mind and take back (revoke) this permission at any time. Even if you take back this permission, St. Jude Children's Research Hospital may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To take back this consent form/permission, you must write to:

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

This permission does not have an expiration date.

Confidentiality

We will protect the confidentiality of your information to the extent reasonably possible.

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.

If you consent to take part in this study, all information learned from the study will be stored, maintained and protected on password protected computer systems that are on secure servers and stored within locked cabinets and offices accessible only to the study team. Your study results will be kept in your research records for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will also be kept for an unknown length of time.

Research data obtained from this study from standard of care tests and procedures and research tests and procedures such as tumor and normal specimens and genetic data, are often shared with the research community using various databases, including those maintained by St. Jude, the federal government, and international collaborative databases. This is to advance scientific discovery, and to satisfy requirements of organizations that fund research, and journals that publish the results of research.

There are two types of databases used for sharing research data. One is a public, unrestricted access database and the other is a controlled access database. Each is described below.

<u>Unrestricted access databases:</u>

The information from research studies using your samples, genetic information, and some health information may be freely available in a public, unrestricted database that anyone can use. A public database could include information on hundreds of thousands of genetic variations in your DNA code, as well as your ethnic group and sex. Summary-level information about all participants included in a dataset, including you, but not genetic data for each individual, may be shared.

Some examples of information that may be shared includes how different genes are associated with different traits or diseases across the many participants in the dataset, or how often certain gene changes are seen across participants from many studies. However, the risk of anyone identifying you

with this information is very low. This public information will not be labeled with your name or other information that could be used to easily identify you.

You will not be notified every time your genomic information is used for research. We also do not know what types of future research will be done with genomic data from this study.

Controlled access databases:

Your individual genomic data and health information may be put in a controlled-access database. This means that only researchers who apply for and get permission to use the information for a specific research project will be able to access the information. Your genomic data and health information will not be labeled with your name or other information that could be used to easily identify you.

Researchers approved to access information in the database must agree to protect the information and not to try to identify you. Examples are the St Jude Cloud, which is run by St. Jude, the database of Genotypes and Phenotypes which is run by the Federal Government, and the European Genome-Phenome archive. These are databases available to researchers to use genomic information from tumor and non-tumor samples to study genetic changes in pediatric diseases.

If you decide you would like to take part in this research study, please ask any questions you have, and read and sign this consent form. You will be given a copy of it to keep. A copy of this consent form will also be put in your patient notes, one will be put with the study records, and one may be sent to the Research Sponsor.

You can have more time to think this over if you are at all unsure.

Thank you for taking the time to read this informed consent document and to consider taking part in this study.

17. Optional Research Tests or Procedures

This section is about optional research studies you can choose to take part in if you participate in the main research study.

You will not get health benefits from any of these optional studies. There are no costs to you or your insurance or other payors. You will not be paid for taking part in these optional studies. If any of the research leads to new tests, drugs, or other commercial products, there is no plan to share any money with you.

We will be closely monitoring and evaluating the immune system of your family member (transplant recipient) before and after the study infusion. To allow us to understand some of the results of your family member's tests, we would like to perform several of the same immune tests before you start the mobilization procedure. If you agree to these tests, they will be collected only once, at the beginning of this study, and require between 9 to 10 teaspoons of blood total. The blood needed for these tests can be obtained in one blood draw or over several days if you prefer. You will not be given the results of these research blood tests.

These research studies are optional. You may choose not to undergo this optional testing and can still take part in this study. If you choose to decline this testing, your decision will not affect your family member's scheduled transplant procedure. There are designated areas with checkboxes at the end of this consent form to mark whether you agree to take part in these voluntary studies. Below is a diagram that gives an overview of these optional tests.

Research Tests or Procedures	**Blood volume totals**	**Frequency of sample collections during this study**
Donor T cell numbers	About 1 teaspoon	Prior to mobilization
Donor T cell production and diversity	About 3 teaspoons	Prior to mobilization
Donor baseline lymphocyte number and function	About 2 teaspoons	Prior to mobilization
Donor baseline phenotype number and function	About 1 teaspoon	Prior to mobilization
Donor baseline immune function- Immunophenotype evaluations	About 1 teaspoon	Prior to mobilization
Donor baseline immune function- T cell function	About 1 teaspoon	Prior to mobilization

By signing this consent form, you are voluntarily and freely donating your blood samples to St. Jude Children's Research Hospital and hereby relinquish all property rights, title, and interest you may have in those samples

The researchers leading the optional studies believe the results will help other people with cancer, HIV, sickle cell disease and other health problems in the future.

The results from these optional research studies will not be added to your medical record nor will you know the results.

You can still take part in the main study even if you say "no" to any or all of these optional studies. If you sign up for but cannot complete any of the optional studies for any reason, you can still take part in the main study. If you choose to take part in these studies later, you will be asked to sign a consent form.

What will happen in the Optional Studies

If you agree to take part in the optional studies, here is what will happen next:

Test/Procedure	Time Point	Purpose
<u>Immune Cell Research Studies: Whole Blood</u> Researchers at St. Jude will perform research tests on blood.	Eight tubes of blood (10 teaspoons or about 50mL) would be taken shortly after enrollment for these studies.	• To learn more about the number and function of the recipient's recovering immune system. • To allow us to better understand some of the recipient's results we will perform the same immune tests on you, as the donor.
Please initial and date your choice: I agree to have my blood used for immune cell research studies		**YES: _____ __/ ___/ ___** **Initials Date** **NO: _____ ___/___/___** **Initials Date**

How will information about me be kept confidential for Future Optional Studies?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take: limiting the uses of the information and the type of information that is shared (especially your personal information), data sharing agreements, and review by oversight groups within St Jude. Often the specimens may be coded to protect your identity before they are shared, and we will keep the key to the code in a secure way.

If data and/or specimens are used or shared with any information that may be likely to identify you, such as your name, address, or medical record number, further institutional review and approval would be required. In these cases, we will review whether additional consent from you is required.

Generally, if your data and/or specimens are used and shared without any personal identifiers or only with information that is less likely to identify you (such as the date of a procedure), further review and approval is not needed, and you will not be contacted.

What if I Change my Mind?

If you decide you no longer want your samples to be used, you can call the study doctor, Dr. Brandon Triplett at 901-595-3300 who will let the researchers know. Then, any sample that remains in the bank will no longer be used. Samples or related information that have already been given to or used by researchers will not be returned or removed.

What happens if some or all of my donated cells (from the apheresis procedure) are not used?

If some or all of your cells are not used, the remainder will be frozen in a very low temperature, secured freezer located at St. Jude. Unused cellular products are destroyed about 5 years after collection or when that cell product is no longer required for therapeutic use by the intended patient. After these time points and based on your choice, unused cells may be donated to St. Jude for research purposes. Or at your expense, the cells can be transferred to an independent storage facility accredited for long-term storage.

Please initial and date your choice below:

Initials ___Date __/__/__ Time _____ AM/PM ___ Yes, I agree to allow my unused donated cell products to be given to St. Jude for research purposes. I understand the staff will not contact me at the time of transfer. Before using the product, they will remove my name and other details linking it to me.

Initials ___Date __/__/__ Time _____ AM/PM ___ No, I do not agree to allow my unused donated cell products to be given to St. Jude for research purposes. I agree to have the cells destroyed without contacting me.

Initials ___Date __/__/__ Time _____ AM/PM ___ No, I do not agree to allow my unused donated cell products to be given to St. Jude for research purposes. Contact me before you stop storing my cells. At my expense, I plan to transfer my cells to an independent storage facility for long-term storage.

If you are planning to transfer your cells, we will contact you in writing, using certified mail or equivalent. We will provide you with contact information for one or more facilities, or you may locate your own. Then you can arrange for the transfer and continued storage of the cells. For this reason, you need to tell St. Jude staff if your address or phone number changes. You may notify St. Jude of changes by calling Patient Registration 901-595-3707 or by sending a note about the change to:

St. Jude Children's Research Hospital
Patient Registration
262 Danny Thomas Place, Mail Stop #114
Memphis, TN 38105
901-595-3707

If we cannot reach you, we will destroy the cells after a reasonable period of time.

18. Signatures

RESEARCH PARTICIPANT STATEMENT (Age 18 years and older):

I have read this consent form or it was read to me. I have been encouraged to ask questions and all of 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 consent form has been given to the participant or his/her representative.

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

_____

Researcher/Designee 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 Signature	Date	Time	(circle one)
_____	_____	_____AM/PM	
Interpreter (if needed) Signature	Date	Time	(circle one)

PLEASE UPLOAD COMPLETED CONSENT FORM TO EPIC.

TCRαβ-DEPLETED PROGENITOR CELL GRAFT WITH ADDITIONAL MEMORY T-CELL DLI, PLUS SELECTED USE OF BLINATUMOMAB, IN NAÏVE T-CELL DEPLETED HAPLOIDENTICAL DONOR HEMATOPOIEITC CELL TRANSPLANTATION FOR HEMATOLOGIC MALIGNANCIES

Note: When we say "you" in this informed consent document, we mean "you or your child." When we talk about research, it can be called a clinical trial, research study (study), or research protocol.

Key Information

To start, we highlight here the risks, benefits and study requirements that we think you should know before deciding if you want to take part in this research study. If you're still interested, we'll then get into more details.

A. Why are you being asked to voluntarily take part in this study?
You are being asked to take part in this clinical trial, a type of research study, because you have a type of cancer that affects the blood or lymphatic system, which can be difficult to treat and is at high risk of coming back after treatment.

B. What is the usual approach to this condition/cancer?
In addition to chemotherapy and radiation, treatment for your cancer includes blood cell transplantation. When patients require blood cell transplantation the first type of transplant to be considered is a matched sibling (brother or sister) donor. For patients who have no matched siblings, a matched unrelated volunteer donor is looked at next. If you have no matched unrelated donor, or if the donor is not available, a mismatched family member donor, such as a parent, sibling, aunt or uncle may be considered.

Once a donor has been found, chemotherapy is given to the recipient to prepare the bone marrow space for the new donor cells. The donor cells are then given to the recipient and find their way to the recipient's bone marrow space and will begin to grow.

C. Why is this study being done?
The purpose of this study is to learn more about newer methods of transplanting blood cells donated by a family member to children with high-risk cancers of the blood or lymphatic system. This includes the effects of the chemotherapy, the transplant cell product and the additional white blood cell (lymphocyte) infusion on the transplant recipient's body, disease and overall survival.

D. What will happen if you decide to take part in this study?
First you will be admitted to the hospital to receive chemotherapy. The donor's blood cells will be collected and you will receive the cell product.

You will continue to be followed in the hospital for about 4 to 8 weeks. The actual number of days you will spend in the hospital will depend on how well your body responds to the treatments and if there are any side effects from the medicines or treatment.

E. What are the research risks and benefits of taking part in this study?
Both your disease, any prior treatment, and this treatment may be associated with potentially life-threatening complications, including death.

The main risks of this treatment are the side effects of:

a. The donor blood cell infusions. The most serious risks related to the blood cell infusions are graft vs. host disease (GVHD), and failure of the new cells to grow after the infusion. GVHD is explained in Part 5 of the consent.

b. The drugs used before and after the infusions. Due to the chemotherapy you may have nausea, vomiting, hair loss and other side effects such as low blood counts, infection and weakness. This is explained in Part 5 of the consent.

Additionally, there is always the serious risk of allergic reactions when taking new medications.

c. The risks of this study treatment on the ability to have children now or in the future are unknown. The effects of this treatment on an unborn or nursing child are also unknown. Therefore, you must not be pregnant, nursing, or attempting to father a child at any time while receiving this treatment.

F. How many people will take part in this study?

We expect that up to 30 transplant recipients will take part in this study over the next few years.

G. What are your options?

1) Taking part in this research study is completely your choice.
2) If you decide to take part in this study, you can change your mind and withdraw from the study at any time.
3) If you decide not to take part in this study, you may still be able to receive care at St. Jude.
4) You may choose to receive standard chemotherapy without treatment.
5) You may choose other experimental treatments using new drugs or methods, if available.
6) You may choose supportive therapy.
7) You may choose no treatment or to seek treatment somewhere else.

If you are still interested in taking part in this research study, HAP2HCT, more detail is provided below in the following pages.

Study Contact Details and Further Information

You are encouraged to ask any questions you wish, before, during or after your treatment. If you have any questions about the study, please speak to your doctor, who will be able to provide you with the up-to-date information about the drug(s)/procedure(s) involved. If there is anything that you do not understand, or if you have any other questions, please contact any of the people below.

Who to talk to for…	You can contact…	At…
• Any new or unexpected symptoms, side effects or discomforts • General study questions • Research related injuries • Any research concerns or complaints • Any medical or surgical treatments done outside of St. Jude such as with your local doctor or another hospital during this study	**Dr. Brandon Triplett or your St. Jude Doctor** 262 Danny Thomas Place Memphis, TN 38105	901-595-3300 (Main Hospital Number)
• Your rights as a research participant • Any research concerns or complaints	**Institutional Review Board (IRB)/Research Participant Advocate** * IRB is a group of scientists and community members who make sure research meets legal and ethical standards * Research Participant Advocates are individuals who are not part of the research study team and are 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 and the IRB.	901-595-4644 or 901-595-1139

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1. Why are you being asked to voluntarily take part in this research study?

You are being asked to take part in this study because you have a type of cancer that affects the blood or lymphatic system, which can be difficult to treat and at a high risk of coming back after treatment. Taking part in this study is completely your choice. Please take your time in deciding and feel free to discuss it with your family, friends, and St. Jude staff. Before agreeing, it is important that you read this informed consent document (consent form) that describes the study. After you understand the study and if you agree to take part, you will be asked to sign this consent form. You will be given a copy to keep.

2. Who is sponsoring this study?

This study is being sponsored by St. Jude Children's Research Hospital. The principal investigator (researcher) in charge of this study is Dr. Brandon Triplett, who can be reached by phone at 901-595-3300, if you have any questions or concerns about this research.

3. What is the purpose of this study?

The purpose of the study is to learn more about the effects (good and bad) of transplanting blood cells donated by a family member and that have been modified in a laboratory, to children and young adults with a high risk cancer that is in remission but is at high risk of relapse. This study is different from previous studies in that a different type of cells (TCRαβ-depleted) will be collected to be given to the recipient. The TCR (T-cell receptor) is a molecule that is found only on T-cells. These T-cell receptors are made up of two proteins that are linked together. About 95% of all T-cells have a TCR that is composed of an alpha protein linked to a beta protein. This blood cell infusion will be followed by an additional infusion of donor memory cells (CD45RA-depleted and CD19+ depleted). This study will be testing the safety and effects of the chemotherapy and the blood cell infusions on the transplant recipient's disease and overall survival.

4. What will be done in this study?

Summaries describing each of these steps are noted below. Your doctor also will provide additional details and answer any questions you may have about these steps. This study treatment includes the following:

- Conditioning treatment (chemotherapy and antibody treatment)
- Donor cell collections from partially matched family member donor
- Donor cell processing
- Donor progenitor cell infusion
- Donor lymphocyte infusion
- Additional progenitor cells and/or donor lymphocyte infusions (if needed)
- Follow up evaluations

Your doctors have reviewed your medical history, clinical status and decided you are eligible to have a transplant. This evaluation included blood tests, kidney, heart, and lung function tests. Before this treatment starts, your doctor will recheck many of these tests and do another complete physical examination to make sure you continue to be able to have this treatment. All these tests are for your clinical care (routine tests) and would be done even if you were not in this study.

Conditioning treatment (Chemotherapy and antibody treatment)

Conditioning is the treatment given to get your body ready to accept the donor blood cells. For this study, chemotherapy will be given to damage your immune system and help to kill your bone marrow. Damaging your bone marrow will help to provide room within your bone marrow space for the new donor cells to settle and grow. On "Day 0" you will have the donor cell infusion. The table below outlines the conditioning treatment you will receive.

Treatment Table:

Medication or Procedure Name	**Schedule**
Rabbit ATG (an antibody)	Days -12, -11, -10
Cyclophosphamide (a chemotherapy)	Day -9
Fludarabine (a chemotherapy)	Days -8, -7, -6, -5, -4
Thiotepa (a chemotherapy)	Day -3
Melphalan (a chemotherapy)	Days -2 and -1
Donor cell infusion	Day 0 and +1(if needed)
Donor lymphocyte infusion (DLI)	Administered once approximately 2 to 3 weeks after Day 0

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

The chemotherapy cyclophosphamide can have a bad side effect causing bleeding and clots in the urine and bladder. You will receive a medicine called mesna to help prevent these effects.

Beginning six days after the primary donor cell infusion you will receive a medication called granulocyte colony stimulating factor (G-CSF or Neupogen®). This medication will be given to help the donor cells

make white blood cells faster so that the immune system is better able to fight infection. G-CSF may be given into your vein or may be given through a small shot under the skin. How long you receive G-CSF will depend on how fast the donor cells grow in your body.

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 treatment and if there are any side effects from the medicines or treatment. Your doctor will discuss any needed changes in your treatment and related medicines with you.

Blood cell collections from partially matched family member

You will receive progenitor (blood making) cells and donor lymphocytes, or white blood cells, collected from the blood of a partially matched family member donor. These cells will be obtained through a procedure called apheresis. A full description of the apheresis procedure will be given to the donor in a separate consent form for him/her to review and sign. The donor's cells will be collected the day before you receive your infusion. You will be given the cells soon after processing and filtering have been done. Sometimes the cell infusions need to be delayed (not given on the planned days) requiring that the donor cells be frozen and stored in a St. Jude laboratory before infusing. However, this is rare.

The cells may need to be collected from the donor's bone marrow through a surgical procedure called a bone marrow harvest. This would be done if the donor is unable to provide enough progenitor 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 cells.

Donor cell processing**.**

Both of the collected donor blood cell products, the one for your transplant and for your lymphocyte infusion, will be processed and filtered in a laboratory at St. Jude using a machine called the CliniMACS™ device. The CliniMACS™ device has been approved for use in the United States by the Food and Drug Administration (FDA). However, the CliniMACS™ process that we will use on the donor blood cells using this device is considered research, or experimental. When processed, the graft which contains the progenitor cells will be infused fresh the same day (most common) or frozen then thawed when you are ready for transplant (rarely).

Donor progenitor cell infusion

You will receive the donor progenitor cell transplant by vein. This infusion will take place in your room. We anticipate that the cells will be given in one infusion, taking about 30 minutes. It is possible, however, that you may need an additional one or two infusions given once per day. Needing more than two infusions is rare. The first day of infusion is called Day 0 and the second infusion day, if needed, is called Day +1. Once in your bloodstream, the progenitor cells will go through your blood to your bone marrow space and should begin to grow.

Donor lymphocyte infusion

Approximately 2 to 3 weeks after your donor progenitor cells have been infused, you will receive a second product that contains mature immune cells to strengthen your developing immune system. This is known as a donor lymphocyte infusion (DLI).

Additional progenitor cells and/or donor lymphocyte infusions (if needed)

We will monitor the number of donor cells in your blood each week after the transplant for about 15 weeks (100 days). The number should increase as the progenitor cells begin to grow in your bone marrow. If the number of donor cells in your blood is lower than needed, we may give you additional lymphocyte products from the same partially matched family member donor.

Lymphocytes are often given to increase the percentage of donor cells in your body. They may also be given if you experience any serious viral infection or if there is any evidence that your disease is coming back (relapse). In some cases, you may be given additional low dose chemotherapy at the time you receive the donor lymphocytes.

Follow-up evaluations

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 donor progenitor cells grow, any complications you have such as infection, and how severe the complications are. We will monitor you closely, both while the donor 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 from the hospital.

Standard testing – Many of the follow up tests and procedures that you will undergo are for your clinical care (routine tests) and would be done even if you were not in this study. At first, these tests will be done often, but will then be done less often as your condition gets better. These tests include but are not limited to:

- Regular medical histories and physical exams
- Blood tests to evaluate your blood counts, nutritional status, organ function, and for infections
- Bone marrow tests to evaluate whether the new donor cells are growing and to evaluate the effect of the treatment on your disease
- X-rays, bone scans, CTs and MRIs to evaluate your condition and the effects the treatment may have had on your body

All of these tests will be used to monitor the effects (good and bad) that the treatment is having on your body and your disease.

Research testing - You will also have blood tests that are experimental (research tests). These blood tests will look at how well the donor cells are growing and their effect on your infection fighting system. You will not be given the results of these research tests. They are described briefly in the table below.

Research Tests to be collected on this study	Total blood volume over the study (12 months)	Frequency of sample collections during this study
T cell production and diversity	About 5 teaspoons	Months 3, 6 and 12 after transplant
Immune cell number and function- Lymphocyte	About 14 teaspoons	Pre-transplant and months 1, 2, 3, 6 and 12 after transplant
Immune cell number and function- Phenotype	About 6 teaspoons	Pre-transplant and months 1, 2, 3, 6 and 12 after transplant
Immunophenotype evaluations	About 6 teaspoons	Pre-transplant and months 1, 2, 3, 6 and 12 after transplant
T cell function studies	About 6 teaspoons	Pre-transplant and months 1, 2, 3, 6 and 12 after transplant

The total treatment and follow-up for this study is about one year. Participants who receive a hematopoietic 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. We want to see if any long-term effects of this research treatment occur.

Optional Research Testing- The study team would also like to perform an optional research test to monitor the ATG antibody levels in the blood. This testing and an option to consent will be described in section 17.

5. What are the risks and benefits of taking part in this study?

a. Risks

Both your disease and 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 donor blood 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 (GVHD). This study treatment can cause some or all of the side effects listed below. There may also be side effects that we cannot predict.

Because the use of the CliniMACS device for the donor blood cell processing is considered experimental, and only a small number of children and young adults in the world have received this study treatment, there may be risks involved with this device that we do not know about right now.

Filtering and processing of the donor 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 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 or yeast in the cells. However, we cannot guarantee that all possible germs or yeast in the cells will be found. You will receive antibiotics and anti-yeast medicines as part of this therapy, if necessary. The chances of developing a severe infection from germs or yeast due to the donor cells is rare.

Side effects of donor cell infusion.

The infusion of donor 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 cells may contain a bacteria or virus that could cause an infection. The cell infusion will be checked for bacteria, and if there is any sign of infection, you will be treated with antibiotics.

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

As noted before, sometimes the donor cell product may need to be frozen and stored until the transplant recipient is ready for the infusion. A frozen product is warmed at room temperature to thaw just before the infusion. When the donor cells are to be frozen, some fluids and a chemical called dimethyl sulfoxide (DMSO) must be added to protect the cells during the freezing and thawing process. If your donor's cells are frozen before infusing, the DMSO that was added may cause you to have a temporary strange taste and smell. You may be able to eat candy, ice cream or popsicles to cover this taste during and/or after the infusion. DMSO may possibly cause your blood pressure to go up, nausea, and vomiting. In very rare cases it may cause your blood pressure to drop, cause changes in your 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 almost always can be treated successfully.

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 cannot be treated. In some cases, patients die of infection.

Graft-versus-host disease.

Graft-versus-host disease (GVHD) is a serious and sometimes fatal side effect of transplantation. 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. Medications are given in this treatment in an effort to help prevent GVHD. If you develop GVHD, the doctors will discuss treatment options with you.

Graft failure/ Graft rejection.

The donor blood cells may not grow in your body. This is called graft failure and it is life-threatening. It is possible that the new donor 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 less than 5 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 progenitor cells which will be requested from the same family donor.

If you experience graft failure or rejection and need additional progenitor cells, your donor may refuse to donate these additional cells or may be unable to undergo an additional 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 transplant recipients 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 (stomach), holding fluid, weight gain, and jaundice which is yellowing of the skin and eyes.

VOD is often mild and causes 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 participants 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.

Loss of privacy

Very rarely, personal information from your records could be given out by accident. This might make you upset, embarrass you, or affect your ability to get insurance. To stop this from happening, we:

- Store records apart from names or other personal information
- Only allow members of the study team to see the records
- Store electronic data only on computers protected with a password and encryption software
- Report study results on the whole group and never identify one single person in any reports

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 antibiotics 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. This is rare but the exact risk is not known, and it is known to be higher in people who have received transplantation than in the general population.

The following pages describe possible side effects specific to each of the 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.

ANTI-THYMOCYTE GLOBULIN (RABBIT) (THYMOGLOBULIN®, RABBIT ATG)

- Fever and chills
- Allergic reactions
- Breathing problems
- Low blood counts
- Skin rash, itching
- Kidney problems
- Chest pain
- Blood pressure changes

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 fluids by mouth or by vein, or by a drug called MESNA.)
- Sterility (unable to have children)
- Second cancers (very rare)
- Lung damage
- Blurred vision
- Abnormal heart beats (at high doses)
- Heart damage
- Mouth sores
- Problems with body fluids and electrolytes

MESNA (Mesnex®)

Stomach pain

Diarrhea and/or loose stools

Headache

Limb and joint pain

Tiredness

Allergic reactions

Low blood pressure

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

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 (unable 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

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

Liver damage

Permanent failure of the bone marrow (very rare)

G-CSF (Filgrastim) (Neupogen®)

- High white blood cell count
- Bone pain
- Bruising at the site of injection
- Fever

Enlarged spleen

Allergic reaction

Abnormal heart beats

The risks of the required genetic/genomic testing are explained below in the Genetic/Genomic section.

b. Benefits

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 help future patients with a cancer such as yours that may be difficult to treat.

6. What are the risks to pregnancy, to an unborn child, and to the ability to have children (fertility) when taking part in this study?

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Some treatments, including (but not limited to) chemotherapy, medicines, radiation, and stem cell transplant can include risks to pregnancy and an unborn child, and can affect your ability to have children (fertility) in the future. These risks can be short-term or permanent. These risks and birth control options are discussed below for both males and females. Please discuss any concerns you may have about future fertility with your doctor. Treatments on this study may involve risks to the pregnancy, the unborn child, or fertility that we currently do not know.

Male Risks:

There may be risks associated with male participants 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.

Female Risks:

The effects of this treatment on an unborn or nursing child are also unknown. Females must not be pregnant or nursing (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.

Fertility (ability to have children) Risks:

The risks of this study treatment on reproduction (ability to have a baby or father a baby) in the future are unknown. We also do not know if there may be unknown long-term effects to your future children.

Birth Control Options:

Participants 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.

7. Can you stop taking part in this study?

a. Can you change your mind about participating in this research study?

You may change your mind about taking part in this research study and stop 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 (chemotherapy and antibody) but *before* the donor cells are infused or have settled in your bone marrow space. If you decide to leave the study, you should talk to your doctor first. He or she will talk to you about health and safety issues. If available, you may continue to receive routine medical care at St. Jude or participate in another study. This decision will not affect your relationship with your doctor at St. Jude.

If you change your mind about participating in this study, samples or related information that have already been used by researchers will not be returned or removed.

b. Can you be taken out of this study without your consent?

You may be taken out of the study without your consent for these 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 cells do not grow in your body or are rejected.
- Your donor develops a change in his/her health status and cannot provide the cells needed for the study.

8. What are you other options and can you have other treatments while taking part in this study?

a. Other Treatment Options

Other options to taking part in this research study include:

- Continue to receive standard therapy without hematopoietic cell transplant.
- Experimental treatments using new therapies, if available.
- Supportive therapy (such as transfusions for low blood counts, medications for pain, antibiotics for infections or hospice care).
- 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. If you decide not to get more treatment, your disease will get worse.

b. Can you participate in other research studies at the same time?

Please check with your study doctor before agreeing to take part in any other research.

c. Other medications, vitamins, and supplements (While in this study, you may not be able to take some or all of the medications or treatments you have been taking for your condition or for other reasons. It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture, or other alternative treatments.

Tell your study doctor about any changes to these during your participation in the research study. Your study doctor will explain to you which treatments or medications need to be stopped for the time you are involved in the research study.

$ 9. How much will it cost you to take part in this study?

If you have health care coverage, we will bill your health care insurer for all standard of care services, tests, and procedures, as applicable. Billing your health care insurer impacts your annual deductible and life-time maximum, if any. This may affect your health care coverage to some extent if you go to another health care provider or institution in the future.

At St. Jude, you will not be responsible for or receive bills for co-pays, co-insurance, deductibles, or similar patient-liability amounts, or for the cost of medical care related to your disease or this study not covered by your health insurer. This includes research-only costs. Research-only tests and procedures (such as optional biopsy or blood samples for biomarker testing) will not be billed to you or your health care insurer.

10. Will you be paid for your time or expenses while taking part in this study?

You will not be paid to take part in this study. Also, your samples and/or 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.

11. What if there is a problem while taking part in this study?

If you are injured from being in this research study, please notify your St. Jude Doctor or the study doctor, **Dr. Brandon Triplett, at 901-595-3300 immediately**. St. Jude will offer you reasonable and necessary medical treatment for that injury. If you need more care than St. Jude can provide or if you prefer to seek treatment elsewhere, we will help you find medical care somewhere else. St. Jude may bill your insurance company or other third parties, if appropriate.

It is not the hospital's policy to provide payment for other types of costs, such as lost wages, disability, or discomfort if you are injured from being in this study. You are not giving up any of your rights by signing this consent form.

12. How will new findings related to your participation in this study be shared with you?

The researcher will tell you of any new information learned during your study participation which might cause you to change your mind about continuing the study. You have the right to learn about the results of the study. If you are interested in learning more about when and how to get the results of this research study, you may contact Dr. Brandon Triplett at 901-595-3300.

13. How will you find out the results of this study?

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
- A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by the 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.

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.

14. Will any genetic tests be done and what are the risks of genetic testing?

As discussed above, we will also obtain samples of your immune cells and other cells during this study. Research performed on your immune cells, and other tissues obtained during this study will include some genetic testing. Genetic testing on material obtained from these samples should help us learn how your immune cells work, and ways to improve transplant therapies in the future.

These additional genetic tests are required and considered research only tests. Results are not reported to you or placed in your electronic medical records. The genetic tests include a partial analysis of genetic material obtained from the samples and may include whole genome sequencing of cells from your body. No direct benefits to participants are expected from these genetic tests.

Because this genetic testing is being done in a research-only lab, you will not receive the results and a copy will not be placed into your electronic medical record.

Risks of Germline Genetic/Genomic Testing

There may be risks to your privacy and the privacy of your relatives from storing your information in a database. Although measures are taken to protect your privacy, we do not know how likely it is that your identity could become re-connected with your genetic and health information, and confidentiality cannot be guaranteed. If your genetic information were re-identified, personal information about you, your health, and your risk of disease could become known to others, and potentially be used to discriminate against or stigmatize you, your family, or your groups. This could also present unknown risks. We believe the chance that this will happen is very small, but we cannot make guarantees. Your privacy and the confidentiality of your data are very important to us; we will make every effort to protect them.

There is a chance that the genomic test results of your normal tissue will show that you have an inherited health condition, or a condition that can be passed down to any children you have. The condition discovered might show that you and possibly other family members are at risk of developing tumors or at risk of developing other health problems unrelated to cancer. It is also possible that testing your normal tissue sample will not find any genetic changes that will affect your current management or future health risks. Sometimes, genetic testing can find gene changes that we do not completely understand. This uncertainty may lead to anxiety or confusion.

After learning your results, you might feel anxious, upset or frustrated. Your doctor will discuss these concerns with you and arrange for needed follow-up, such as with the Genetics Service or other support services (social work, spiritual care, or psychology).

As opposed to a research genomic test, any clinical genomic test report comes from a CLIA certified laboratory and the results will be placed into your electronic medical record and may be seen by you, your care team, and other doctors and health care workers at St. Jude or other facilities that obtain your medical record with your permission or legal authority.

Currently, the U.S. law known as the "Genetic Information Nondiscrimination Act" (GINA) prohibits discrimination based on genetic findings in some circumstances:

a. GINA prohibits health care insurers from requesting or requiring genetic information of an individual or an individual's family members or using genetic information for decisions about health insurance coverage or rates, or to exclude preexisting conditions.
b. In companies of 15 or more employees, GINA prohibits employment and employee-related decisions from being made on the basis of genetic information of an individual or an individual's family members.

GINA protections do not apply to:

a. the presence of disease or a health disorder,
b. life insurance, long-term care insurance, or disability insurance. These insurance companies consider may this information in making insurance decisions affecting you,
c. both health care plans and employment from companies employing fewer than 15 people, and
d. people in the military.
e. There are other health plans that GINA does not apply. Please ask your study doctor if you have any questions.

15. What about identifiable private information and identifiable biospecimens (blood, tissue, urine, cells, and any type of data and/or samples) obtained from you during the study?

If you choose to take part in this study, your data and/or specimens will be used to answer the research question(s) and to publish the findings of this study. 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. You will not own your research data and/or specimens. If researchers use your data and/or specimens to create a new product or idea, including those that may have commercial value, you will not benefit financially. There is no plan to share any money with you.

St. Jude's researchers and their collaborators will store the data and specimens collected in this study in electronic databases and other locations and will store specimens in the biorepository or other locations. They may use the data and/or specimens collected in this study for future research purposes and may share some of the data or specimens with others without seeking further consent from you. You may not receive results from that future research.

Sharing data and/or specimens is part of research. It may increase what can be learned from this study and future studies. Often data sharing is required as a condition of funding or for publishing study results. It is also needed to allow other researchers to validate study findings and to come up with new ideas.

Your data and/or specimens may be shared with government agencies, research collaborators, and other researchers and organizations conducting research that may not be related to this study. Your data may also be put in government or other databases/repositories as mentioned in the section above.

Future research using your samples and data is likely to include studies that look at genomic and genetic information to understand causes and cures for health conditions. Because science constantly advances, we do not yet know what other future uses of research data and/or specimens may include. There is no time-limit on sharing of information.

This future research may be unrelated to the current study and may include outside researchers and organizations from around the world. These organizations may include for-profit companies conducting medical research. We or others who distribute data or samples may be paid for data or samples, including yours. You will not receive payment if this happens.

St. Jude will do its best to protect and maintain your data and/or specimens in a safe way. One of the ways we protect your data and/or specimens is by limiting the uses of the information and the type of information that is shared, especially your personal information. This may occur through data sharing agreements and review by oversight groups within St Jude. Often the data and specimens may be coded to protect your identity before they are shared, and we will keep the key to the code in a secure way.

If data and/or specimens are used or shared with any information that may be likely to identify you, such as your name, address, or medical record number, further institutional review and approval would be required. In these cases, we will review whether additional consent from you is required.

Generally, if your data and/or specimens are used and shared without any personal identifiers or only with information that is less likely to identify you (such as the date of a procedure), further review and approval is not needed, and you will not be contacted.

Data sharing could change over time and may continue after the study ends.

The use and sharing of your data and/or specimens is required for participation in this research study. The purpose of research is to learn and discover new information to make improvements to patient care and/or treatments. To make these improvements, research results must be shared with others. By agreeing to take part in research studies, you are agreeing for your information or data to be used and shared with others. If you are generally not comfortable with the use and sharing of your data and/or specimens in future research as explained this consent, you should talk with your doctor before agreeing to take part in this study.

16. What about permission to use your data/information (HIPAA Privacy Rule), privacy and confidentiality?

Permission to Use Your Data/Information- HIPAA Privacy Rule and Privacy

The HIPAA Privacy Rule defines the situations in which PHI (protected health information) may be used or given to someone outside of the hospital to be used or released for research and other purposes. PHI includes information such as your name, MRN, date of birth, or other identifying information, including research information placed in your medical record.

To do this research, St. Jude Children's Research Hospital (St. Jude) will need to collect, use, and share your private health information. St. Jude is required by law to protect your health information. By signing this consent form, you give St. Jude permission to use and/or release (share) your private health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

If you sign this consent form, you give permission to all researchers and their staff involved in the study at St. Jude to use or release (share) your health information that identifies you for the research study described in this document.

The health information that we may use or release includes things learned from the procedures and treatments describes in this consent form, as well as all information from your medical record (which may include information such as HIV status, drug, alcohol, or STD treatment, genetic test results, or mental health condition and/or treatment, physical examinations, and lab tests).

If you sign this consent form, you give St. Jude permission to share your information for future research studies about disease or advancing science and for future unspecified research. You also give permission for us to place this information on databases as described below under Privacy and Confidentiality.

Information from research testing will be analyzed in a CLIA-certified (medical) laboratory or a research-only laboratory. By signing, you give St. Jude permission to put your research information obtained from a CLIA-certified laboratory into your medical record. Results from research-only laboratories will not be put into your medical record and will not generally be available to you or your doctor.

If you sign this document, you give St. Jude permission to share your information for future research studies and for the placement of information in databases as described in #14 of this consent form. By signing, you will also give St. Jude permission to put your research information, including testing, imaging, genomic and genetic information, other information and studies, and other sensitive information in your medical record (unless the research information is from a research-only laboratory). Any information placed in the medical record becomes a permanent part of your record, is kept indefinitely, and is not protected by a Certificate of Confidentiality (Certificate of Confidentiality, if included with this study, is described below under Privacy and Confidentiality). It is protected like any other part of your medical record as described in the Notice of Privacy Practices. You have the right to see, copy, and ask for changes to your PHI that will be used or shared. However, research information may not be available until after the end of the study.

When you first registered at St. Jude, you received a copy of the St. Jude Notice of Privacy Practices. It tells how your PHI, including research information placed in your medical record, may be used or given to someone outside of St. Jude. You have the right to read the Notice of Privacy Practices before you sign this consent form. It may have changes 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

A decision to take part in this research means that you agree to let the research team use and share your PHI with other researchers for purposes of 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.

Federal agencies such as the Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), the National Institutes of Health (NIH), and St. Jude Children's Research Hospital Institutional Review Board (IRB), your insurance company and other health benefits plan (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.

Information about you may also be shared with representatives from the Miltenyi Biotec Corporation, the manufacturer of the investigational CliniMACS blood cell selection device. This information will include any information related to how well the device works, if there is a malfunction and any related problems that you may experience as a result of the malfunction of the device.

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 a worldwide research organization of scientists and doctors who study important issues in transplantation.

Your donor blood 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 for monitoring the clinical and laboratory activities of institutions that provide research and treatment with certain blood cell products including blood progenitor 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.

Because this information may be linked to you, absolute privacy cannot be guaranteed.

By signing this consent form, you are allowing your data and/or biological sample 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).
- 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.
- Other committees or people involved in overseeing research studies.
- Miltenyi Biotec, the maker of the CliniMACS device system

The people who may view, request, receive, or use your private health information include St. Jude researchers and their staff, and other doctors, nurses, and staff members. Additionally, St. Jude may share your information with other people or groups of people. These include:

- Transplant related oversight agencies or registries that may receive and process PHI (CIBMTR, FACT and NMDP); and/or
- St. Jude Institutional Review Board and St. Jude Institutional Biosafety Committee

You do not have to sign this consent form which gives your permission, but if you do not, you may not receive research-related treatment.

Please note that you may change your mind and take back (revoke) this permission at any time. Even if you take back this permission, St. Jude Children's Research Hospital may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To take back this consent form/permission, you must write to:

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

This permission does not have an expiration date.

Confidentiality

We will protect the confidentiality of your information to the extent reasonably possible.

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.

If you consent to take part in this study, all information learned from the study will be stored, maintained and protected on password protected computer systems that are on secure servers and stored within locked cabinets and offices accessible only to the study team. Your study results will be kept in your research records for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will also be kept for an unknown length of time.

Research data obtained from this study from standard of care tests and procedures and research tests and procedures such as tumor and normal specimens and genetic data, are often shared with the research community using various databases, including those maintained by St. Jude, the federal government, and international collaborative databases. This is to advance scientific discovery, and to satisfy requirements of organizations that fund research, and journals that publish the results of research.

There are two types of databases used for sharing research data. One is a public, unrestricted access database and the other is a controlled access database. Each is described below.

<u>Unrestricted access databases:</u>

The information from research studies using your samples, genetic information, and some health information may be freely available in a public, unrestricted database that anyone can use. A public database could include information on hundreds of thousands of genetic variations in your DNA code, as well as your ethnic group and sex. Summary-level information about all participants included in a dataset, including you, but not genetic data for each individual, may be shared.

Some examples of information that may be shared includes how different genes are associated with different traits or diseases across the many participants in the dataset, or how often certain gene

changes are seen across participants from many studies. However, the risk of anyone identifying you with this information is very low. This public information will not be labeled with your name or other information that could be used to easily identify you.

You will not be notified every time your genomic information is used for research. We also do not know what types of future research will be done with genomic data from this study.

Controlled access databases:

Your individual genomic data and health information may be put in a controlled-access database. This means that only researchers who apply for and get permission to use the information for a specific research project will be able to access the information. Your genomic data and health information will not be labeled with your name or other information that could be used to easily identify you.

Researchers approved to access information in the database must agree to protect the information and not to try to identify you. Examples are the St Jude Cloud, which is run by St. Jude, the database of Genotypes and Phenotypes which is run by the Federal Government, and the European Genome-Phenome archive. These are databases available to researchers to use genomic information from tumor and non-tumor samples to study genetic changes in pediatric diseases.

If you decide you would like to take part in this research study, please ask any questions you have, and read and sign this consent form. You will be given a copy of it to keep. A copy of this consent form will also be put in your patient notes, one will be put with the study records, and one may be sent to the Research Sponsor.

You can have more time to think this over if you are at all unsure.

Thank you for taking the time to read this informed consent document and to consider taking part in this study.

17. Optional Research Tests or Procedures

This section is about optional research studies you can choose to take part in if you participate in the main research study.

You will not get health benefits from any of these optional studies. There are no costs to you or your insurance or other payors. You will not be paid for taking part in these optional studies. If any of the research leads to new tests, drugs, or other commercial products, there is no plan to share any money with you.

Optional ATG PK Research Test

This research test is optional. You may choose not to undergo this optional testing and can still take part in this study. The purpose of this optional research test is to evaluate drug exposure and to determine the length of time that ATG remains active following HCT in recipient participants of this study through pharmacokinetic (PK) testing. There is a designated area with checkboxes at the end of this consent form to mark whether you agree to take part in this voluntary study.

Below is a diagram that gives an overview of this optional test.

Optional Research Test to be collected on this study	Blood volume total for length of study	Frequency of sample collection during this study
ATG PK	About 3 teaspoons	Pre and Post-3rd dose on Day-10, Once each on Days -8, -7, -5, -3, 0, +7, +14

By signing this consent form, you are voluntarily and freely donating your blood samples to St. Jude Children's Research Hospital and hereby relinquish all property rights, title, and interest you may have in this sample.

The researchers leading the optional studies believe the results will help other people with cancer, HIV, sickle cell disease and other health problems in the future.

The results from these optional research studies will not be added to your medical record nor will you know the results.

You can still take part in the main study even if you say "no" to the optional study. If you sign up for but cannot complete any of the optional study for any reason, you can still take part in the main study. If you choose to take part in these studies later, you will be asked to sign a consent form.

What will happen in this Optional Study)?

If you agree to take part in this optional study, here is what will happen next:

Test/Procedure	Time Point	Purpose
ATG PK Researchers at St. Jude will perform research tests on blood.	Nine total tubes of blood (3 teaspoons or about 18mL) would be taken Pre and Post-3rd dose on Day -10, Once each on Days -8, -7, -5, -3, 0, +7 and +14.	• To evaluate drug exposure and to determine the length of time that ATG remains active following HCT.
Please initial and date your choice: I agree to have my blood used for ATG PK optional research study		**YES: _____ __/ ___/ ___** **Initials Date** **NO: _____ ___/___/___** **Initials Date**

What if I Change my Mind?

If you decide you no longer want your samples to be used, you can call the study doctor, Dr. Brandon Triplett at 901-595-3300,*)* who will let the researchers know. Then, any sample that remains in the bank will no longer be used. Samples or related information that have already been given to or used by researchers will not be returned or removed.

18. Signatures

PARENT/Legal GUARDIAN STATEMENT (Required for participants younger than 18 years)

I have read this consent form or it was read to me. I have been encouraged to ask questions and all my questions have been answered. I give my 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 7-17 years old)

□ The research was explained to the minor participant aged 7 to 13 years in age-appropriate terms and the minor verbally agreed to take part in the study.

□ Minor Age 14 to 17 years old Assent Signature:

I have read this consent form or it was read to me and discussed in a way that I could understand. I have been encouraged to ask questions and all of my questions were answered. I agree to take part in this research study.

_____ _____ _____AM/PM

Minor Assent Signature Date Time (circle one)

□ 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 STATEMENT (Age 18 years and older):

I have read this consent form or it was read to me. I have been encouraged to ask questions and all of 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 consent form has been given to the participant or his/her representative.

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

_____

Researcher/Designee 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 Signature	Date	Time	(circle one)
_____	_____	_____AM/PM	
Interpreter (if needed) Signature	Date	Time	(circle one)

PLEASE UPLOAD COMPLETED CONSENT FORM TO EPIC.

Initial version dated: 03/01/2024
Consent document date: 03/01/2024

TCRαβ-DEPLETED PROGENITOR CELL GRAFT WITH ADDITIONAL MEMORY T-CELL DLI, PLUS SELECTED USE OF BLINATUMOMAB, IN NAÏVE T-CELL DEPLETED HAPLOIDENTICAL DONOR HEMATOPOIEITC CELL TRANSPLANTATION FOR HEMATOLOGIC MALIGNANCIES

Note: When we say "you" in this informed consent document, we mean "you or your child." When we talk about research, it can be called a clinical trial, research study (study), or research protocol.

Key Information

To start, we highlight here the risks, benefits and study requirements that we think you should know before deciding if you want to take part in this research study. If you're still interested, we'll then get into more details.

A. Why are you being asked to voluntarily take part in this study?
You are being asked to take part in this clinical trial, a type of research study, because you have a type of cancer that affects the blood or lymphatic system, which can be difficult to treat and is at high risk of coming back after treatment.

B. What is the usual approach to this condition/cancer?
In addition to chemotherapy and radiation, treatment for your cancer includes blood cell transplantation. When patients require blood cell transplantation the first type of transplant to be considered is a matched sibling (brother or sister) donor. For patients who have no matched siblings, a matched unrelated volunteer donor is looked at next. If you have no matched unrelated donor, or if the donor is not available, a mismatched family member donor, such as a parent, sibling, aunt, or uncle may be considered.

Once a donor has been found, chemotherapy is given to the recipient to prepare the bone marrow space for the new donor cells. The donor cells are then given to the recipient and find their way to the recipient's bone marrow space and will begin to grow.

C. Why is this study being done?
The purpose of this study is to learn more about newer methods of transplanting blood cells donated by a family member to children with high-risk cancers of the blood or lymphatic system. This includes the effects of the chemotherapy, the transplant cell product, and the additional white blood cell (lymphocyte) infusion on the transplant recipient's body, disease, and overall survival.

D. What will happen if you decide to take part in this study?
First you will be admitted to the hospital to receive chemotherapy. The donor's blood cells will be collected and you will receive the cell product.

You will continue to be followed in the hospital for about 4 to 8 weeks. The actual number of days you will spend in the hospital will depend on how well your body responds to the treatments and if there are any side effects from the medicines or treatment.

E. What are the research risks and benefits of taking part in this study?
Both your disease, any prior treatment, and this treatment may be associated with potentially life-threatening complications, including death.

The main risks of this treatment are the side effects of:

a. The donor blood cell infusions. The most serious risks related to the blood cell infusions are graft vs. host disease (GVHD), and failure of the new cells to grow after the infusion. GVHD is explained in Part 5 of the consent.
b. The drugs used before and after the infusions. Due to the chemotherapy, you may have nausea, vomiting, hair loss and other side effects such as low blood counts, infection, and weakness. This is explained in Part 5 of the consent.
Additionally, there is always the serious risk of allergic reactions when taking new medications.
c. The risks of this study treatment on the ability to have children now or in the future are unknown. The effects of this treatment on an unborn or nursing child are also unknown. Therefore, you must not be pregnant, nursing, or attempting to father a child at any time while receiving this treatment.

F. How many people will take part in this study?
We expect that up to 30 transplant recipients will take part in this study over the next few years.

G. What are your options?
1) Taking part in this research study is completely your choice.
2) If you decide to take part in this study, you can change your mind and withdraw from the study at any time.
3) If you decide not to take part in this study, you may still be able to receive care at St. Jude.
4) You may choose to receive standard chemotherapy without treatment.
5) You may choose other experimental treatments using new drugs or methods, if available.
6) You may choose supportive therapy.
7) You may choose no treatment or to seek treatment somewhere else.

If you are still interested in taking part in this research study, HAP2HCT, more detail is provided below in the following pages.

Study Contact Details and Further Information

You are encouraged to ask any questions you wish, before, during or after your treatment. If you have any questions about the study, please speak to your doctor, who will be able to provide you with the up-to-date information about the drug(s)/procedure(s) involved. If there is anything that you do not understand, or if you have any other questions, please contact any of the people below.

Who to talk to for…	You can contact…	At…
• Any new or unexpected symptoms, side effects or discomforts • General study questions • Research related injuries • Any research concerns or complaints • Any medical or surgical treatments done outside of St. Jude such as with your local doctor or another hospital during this study	**Dr. Brandon Triplett or your St. Jude Doctor** 262 Danny Thomas Place Memphis, TN 38105	901-595-3300 (Main Hospital Number)
• Your rights as a research participant • Any research concerns or complaints	**Institutional Review Board (IRB)/Research Participant Advocate** * IRB is a group of scientists and community members who make sure research meets legal and ethical standards * Research Participant Advocates are individuals who are not part of the research study team and are 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 and the IRB.	901-595-4644 or 901-595-1139

Table of Contents

1. Why are you being asked to voluntarily take part in this research study?

You are being asked to take part in this study because you have a type of cancer that affects the blood or lymphatic system, which can be difficult to treat and at a high risk of coming back after treatment. Taking part in this study is completely your choice. Please take your time in deciding and feel free to discuss it with your family, friends, and St. Jude staff. Before agreeing, it is important that you read this informed consent document (consent form) that describes the study. After you understand the study and if you agree to take part, you will be asked to sign this consent form. You will be given a copy to keep.

2. Who is sponsoring this study?

This study is being sponsored by St. Jude Children's Research Hospital. The principal investigator (researcher) in charge of this study is Dr. Brandon Triplett, who can be reached by phone at 901-595-3300, if you have any questions or concerns about this research.

3. What is the purpose of this study?

The purpose of the study is to learn more about the effects (good and bad) of transplanting blood cells donated by a family member and that have been modified in a laboratory, to children and young adults with a high risk cancer that is in remission but is at high risk of relapse. This study is different from previous studies in that a different type of cells (TCRαβ-depleted) will be collected to be given to the recipient. The TCR (T-cell receptor) is a molecule that is found only on T-cells. These T-cell receptors are made up of two proteins that are linked together. About 95% of all T-cells have a TCR that is composed of an alpha protein linked to a beta protein. This blood cell infusion will be followed by an additional infusion of donor memory cells (CD45RA-depleted and CD19+ depleted). This study will be testing the safety and effects of the chemotherapy and the blood cell infusions on the transplant recipient's disease and overall survival.

4. What will be done in this study?

Summaries describing each of these steps are noted below. Your doctor will also provide additional details and answer any questions you may have about these steps. This study treatment includes the following:

- Conditioning treatment (chemotherapy and antibody treatment)
- Donor cell collections from partially matched family member donor
- Donor cell processing
- Donor progenitor cell infusion
- Donor lymphocyte infusion
- Additional progenitor cells and/or donor lymphocyte infusions (if needed)
- Follow up evaluations

Your doctors have reviewed your medical history and clinical status and decided you are eligible to have a transplant. This evaluation included blood tests, kidney, heart, and lung function tests. Before this treatment starts, your doctor will recheck many of these tests and do another complete physical examination to make sure you continue to be able to have this treatment. All these tests are for your clinical care (routine tests) and would be done even if you were not in this study.

Conditioning treatment (Chemotherapy and antibody treatment)

Conditioning is the treatment given to get your body ready to accept the donor blood cells. For this study, chemotherapy will be given to damage your immune system and help to kill your bone marrow. Damaging your bone marrow will help to provide room within your bone marrow space for the new donor cells to settle and grow. On "Day 0" you will have the donor cell infusion. The table below outlines the conditioning treatment you will receive.

Treatment Table:

Medication or Procedure Name	**Schedule**
Rabbit ATG (an antibody)	Days -12, -11, -10
Cyclophosphamide (a chemotherapy)	Day -9
Fludarabine (a chemotherapy)	Days -8, -7, -6, -5, -4
Thiotepa (a chemotherapy)	Day -3
Melphalan (a chemotherapy)	Days -2 and -1
Donor cell infusion	Day 0 and +1(if needed)
Donor lymphocyte infusion (DLI)	Administered once approximately 2 to 3 weeks after Day 0
Blinatumomab (an antibody)	Starting at least 4 weeks after DLI, no later than Day +180

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

The chemotherapy cyclophosphamide can have a bad side effect causing bleeding and clots in the urine and bladder. You will receive a medicine called mesna to help prevent these effects.

Beginning six days after the primary donor cell infusion you will receive a medication called granulocyte colony stimulating factor (G-CSF or Neupogen®). This medication will be given to help the donor cells make white blood cells faster so that the immune system is better able to fight infection. G-CSF may be given into your vein or may be given through a small shot under the skin. How long you receive G-CSF will depend on how fast the donor cells grow in your body.

Your cancer type falls into a group of cancers that are described as a B-cell malignancy (CD19+). Therefore, an additional medication, called blinatumomab, will be added to your treatment at least 4 weeks after you receive your donor lymphocyte infusion. Blinatumomab is given as a continuous infusion over a period of 4 weeks. The first 3 days of blinatumomab will most often be given in the hospital; thereafter you may continue to receive blinatumomab in the medicine room as an outpatient. The infusion will require the use of a "minipump" that you will carry with you at all times. Your ability to move around, wear regular clothes, play and do most of the things that you like to do should not be affected too much. You will be given a shoulder or belt bag which will hold the pump and infusion bag. The pump will be set up by trained persons, like your doctors and clinic nurses. You should not change or program the settings of the infusion pump. If you have any reactions while receiving blinatumomab you may receive additional medications to treat or prevent those reactions.

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 treatment and if there are any side effects from the medicines or treatment. Your doctor will discuss any needed changes in your treatment and related medicines with you.

Blood cell collections from partially matched family member

You will receive progenitor (blood making) cells and donor lymphocytes, or white blood cells, collected from the blood of a partially matched family member donor. These cells will be obtained through a procedure called apheresis. A full description of the apheresis procedure will be given to the donor in a separate consent form for him/her to review and sign. The donor's cells will be collected the day before you receive your infusion. You will be given the cells soon after processing and filtering have been done. Sometimes the cell infusions need to be delayed (not given on the planned days) requiring that the donor cells be frozen and stored in a St. Jude laboratory before infusing. However, this is rare.

The cells may need to be collected from the donor's bone marrow through a surgical procedure called a bone marrow harvest. This would be done if the donor is unable to provide enough progenitor 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 cells.

Donor cell processing**.**

Both of the collected donor blood cell products, the one for your transplant and for your lymphocyte infusion, will be processed and filtered in a laboratory at St. Jude using a machine called the CliniMACS™ device. The CliniMACS™ device has been approved for use in the United States by the Food and Drug Administration (FDA). However, the CliniMACS™ process that we will use on the donor blood cells using this device is considered research, or experimental. When processed, the graft which contains the progenitor cells will be infused fresh the same day (most common) or frozen then thawed when you are ready for transplant (rarely).

Donor progenitor cell infusion

You will receive the donor progenitor cell transplant by vein. This infusion will take place in your room. We anticipate that the cells will be given in one infusion, taking about 30 minutes. It is possible, however, that you may need an additional one or two infusions given once per day. Needing more than two infusions is rare. The first day of infusion is called Day 0 and the second infusion day, if needed, is called Day +1. Once in your bloodstream, the progenitor cells will go through your blood to your bone marrow space and should begin to grow.

Donor lymphocyte infusion

Approximately 2 to 3 weeks after your donor progenitor cells have been infused, you will receive a second product that contains mature immune cells to strengthen your developing immune system. This is known as a donor lymphocyte infusion (DLI).

Additional progenitor cells and/or donor lymphocyte infusions (if needed)

We will monitor the number of donor cells in your blood each week after the transplant for about 15 weeks (100 days). The number should increase as the progenitor cells begin to grow in your bone marrow. If the number of donor cells in your blood is lower than needed, we may give you additional lymphocyte products from the same partially matched family member donor.

Lymphocytes are often given to increase the percentage of donor cells in your body. They may also be given if you experience any serious viral infection or if there is any evidence that your disease is coming back (relapse). In some cases, you may be given additional low dose chemotherapy at the time you receive the donor lymphocytes.

Follow-up evaluations

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 donor progenitor cells grow, any complications you have such as infection, and how severe the complications are. We will monitor you closely, both while the donor 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 from the hospital.

Standard testing – Many of the follow up tests and procedures that you will undergo are for your clinical care (routine tests) and would be done even if you were not in this study. At first, these tests will be done often, but will then be done less often as your condition gets better. These tests include but are not limited to:

- Regular medical histories and physical exams
- Blood tests to evaluate your blood counts, nutritional status, organ function, and for infections
- Bone marrow tests to evaluate whether the new donor cells are growing and to evaluate the effect of the treatment on your disease
- X-rays, bone scans, CTs and MRIs to evaluate your condition and the effects the treatment may have had on your body

All of these tests will be used to monitor the effects (good and bad) that the treatment is having on your body and your disease.

Research testing - You will also have blood tests that are experimental (research tests). These blood tests will look at how well the donor cells are growing and their effect on your infection fighting system. You will not be given the results of these research tests. They are described briefly in the table below.

Research Tests to be collected on this study	Total blood volume over the study (12 months)	Frequency of sample collections during this study
T cell production and diversity	About 5 teaspoons	Months 3, 6 and 12 after transplant
Immune cell number and function- Lymphocyte	About 14 teaspoons	Pre-transplant and months 1, 2, 3, 6 and 12 after transplant
Immune cell number and function- Phenotype	About 6 teaspoons	Pre-transplant and months 1, 2, 3, 6 and 12 after transplant
Immunophenotype evaluations	About 6 teaspoons	Pre-transplant and months 1, 2, 3, 6 and 12 after transplant
T cell function studies	About 6 teaspoons	Pre-transplant and months 1, 2, 3, 6 and 12 after transplant

The total treatment and follow-up for this study is about one year. Participants who receive a hematopoietic 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. We want to see if any long-term effects of this research treatment occur.

Optional Research Testing- The study team would also like to perform an optional research test to monitor the ATG antibody levels in the blood. This testing and an option to consent will be described in section 17.

5. What are the risks and benefits of taking part in this study?

a. Risks

Both your disease and 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 donor blood 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 (GVHD). This study treatment can cause some or all of the side effects listed below. There may also be side effects that we cannot predict.

Because the use of the CliniMACS device for the donor blood cell processing is considered experimental, and only a small number of children and young adults in the world have received this study treatment, there may be risks involved with this device that we do not know about right now.

Filtering and processing of the donor 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 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 or yeast in the cells. However, we cannot guarantee that all possible germs or yeast in the cells will be found. You will receive antibiotics and anti-yeast medicines as part of this therapy, if necessary. The chances of developing a severe infection from germs or yeast due to the donor cells is rare.

Side effects of donor cell infusion.

The infusion of donor 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 cells may contain a bacteria or virus that could cause an infection. The cell infusion will be checked for bacteria, and if there is any sign of infection, you will be treated with antibiotics.

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

As noted before, sometimes the donor cell product may need to be frozen and stored until the transplant recipient is ready for the infusion. A frozen product is warmed at room temperature to thaw just before the infusion. When the donor cells are to be frozen, some fluids and a chemical called dimethyl sulfoxide (DMSO) must be added to protect the cells during the freezing and thawing process. If your donor's cells are frozen before infusing, the DMSO that was added may cause you to have a temporary strange taste and smell. You may be able to eat candy, ice cream or popsicles to cover this taste during and/or after the infusion. DMSO may possibly cause your blood pressure to go up, nausea, and vomiting. In very rare cases it may cause your blood pressure to drop, cause changes in your 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 almost always can be treated successfully.

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 cannot be treated. In some cases, patients die of infection.

Graft-versus-host disease.

Graft-versus-host disease (GVHD) is a serious and sometimes fatal side effect of transplantation. 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. Medications are given in this treatment in an effort to help prevent GVHD. If you develop GVHD, the doctors will discuss treatment options with you.

Graft failure/ Graft rejection.

The donor blood cells may not grow in your body. This is called graft failure and it is life-threatening. It is possible that the new donor 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 less than 5 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 progenitor cells which will be requested from the same family donor.

If you experience graft failure or rejection and need additional progenitor cells, your donor may refuse to donate these additional cells or may be unable to undergo an additional 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 transplant recipients 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 (stomach), holding fluid, weight gain, and jaundice which is yellowing of the skin and eyes.

VOD is often mild and causes 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 participants 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.

Loss of privacy

Very rarely, personal information from your records could be given out by accident. This might make you upset, embarrass you, or affect your ability to get insurance. To stop this from happening, we:

- Store records apart from names or other personal information
- Only allow members of the study team to see the records
- Store electronic data only on computers protected with a password and encryption software
- Report study results on the whole group and never identify one single person in any reports

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 antibiotics 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. This is rare but the exact risk is not known, and it is known to be higher in people who have received transplantation than in the general population.

The following pages describe possible side effects specific to each of the 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.

ANTI-THYMOCYTE GLOBULIN (RABBIT) (THYMOGLOBULIN®, RABBIT ATG)

- Fever and chills
- Allergic reactions
- Breathing problems
- Low blood counts
- Skin rash, itching
- Kidney problems
- Chest pain
- Blood pressure changes

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 fluids by mouth or by vein, or by a drug called MESNA.)
- Sterility (unable to have children)

Second cancers (very rare)

Lung damage

Blurred vision

Abnormal heart beats (at high doses)

Heart damage

Mouth sores

Problems with body fluids and electrolytes

MESNA (Mesnex®)

Stomach pain

Diarrhea and/or loose stools

Headache

Limb and joint pain

Tiredness

Allergic reactions

Low blood pressure

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

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 (unable 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

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

Liver damage

Permanent failure of the bone marrow (very rare)

G-CSF (Filgrastim) (Neupogen®)

- High white blood cell count
- Bone pain
- Bruising at the site of injection
- Fever

Enlarged spleen

Allergic reaction

Abnormal heart beats

BLINATUMOMAB (Blincyto™)

- Fever
- Neurotoxicity including, tremors, seizures, confusion, disorientation, difficulty speaking or slurred speech, dizziness, loss of balance, or loss of consciousness
- Headache
- Low blood counts resulting in a higher than usual chance of bleeding, fever, or infection
- Nausea and/or vomiting
- Diarrhea or constipation
- Fatigue
- Chills
- Shortness of breath
- Abdominal pain
- Chest pain
- Bone and joint pain
- Back pain
- Pain in arms, legs, and hands
- Cough

- Rash
- Difficulty falling and/or staying asleep
- Weight gain
- Swelling of hands, legs, ankles, feet, face or trunk
- Low blood pressure
- Increased blood glucose, liver enzymes
- Decreased levels of potassium, magnesium
- Decreased appetite
- Tumor lysis syndrome (a group of complications caused by the breakdown of tumor cells after cancer treatment, in more severe forms it can lead to kidney failure, abnormal heart rhythm, and death)
- Cytokine release syndrome (syndrome caused by the body's release of substances called cytokines after receiving medications such as Blinatumomab, symptoms include: difficulty breathing or swallowing, wheezing, flushing, hives or rash, fever, headache, nausea, lightheadedness, shaking or chills

The risks of the required genetic/genomic testing are explained below in the Genetic/Genomic section.

b. Benefits

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 help future patients with a cancer such as yours that may be difficult to treat.

6. What are the risks to pregnancy, to an unborn child, and to the ability to have children (fertility) when taking part in this study?

Some treatments, including (but not limited to) chemotherapy, medicines, radiation, and stem cell transplant can include risks to pregnancy and an unborn child, and can affect your ability to have children (fertility) in the future. These risks can be short-term or permanent. These risks and birth control options are discussed below for both males and females. Please discuss any concerns you may have about future fertility with your doctor. Treatments on this study may involve risks to the pregnancy, the unborn child, or fertility that we currently do not know.

Male Risks:

There may be risks associated with male participants 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.

Female Risks:

The effects of this treatment on an unborn or nursing child are also unknown. Females must not be pregnant or nursing (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.

Fertility (ability to have children) Risks:

The risks of this study treatment on reproduction (ability to have a baby or father a baby) in the future are unknown. We also do not know if there may be unknown long-term effects to your future children.

Birth Control Options:

Participants 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.

7. Can you stop taking part in this study?

a. Can you change your mind about participating in this research study?

You may change your mind about taking part in this research study and stop 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 (chemotherapy and antibody) but *before* the donor cells are infused or have settled in your bone marrow space. If you decide to leave the study, you should talk to your doctor first. He or she will talk to you about health and safety issues. If available, you may continue to receive routine medical care at St. Jude or participate in another study. This decision will not affect your relationship with your doctor at St. Jude.

If you change your mind about participating in this study, samples or related information that have already been used by researchers will not be returned or removed.

b. Can you be taken out of this study without your consent?

You may be taken out of the study without your consent for these 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 cells do not grow in your body or are rejected.
- Your donor develops a change in his/her health status and cannot provide the cells needed for the study.

8. What are you other options and can you have other treatments while taking part in this study?

a. Other Treatment Options

Other options to taking part in this research study include:

- Continue to receive standard therapy without hematopoietic cell transplant.
- Experimental treatments using new therapies, if available.
- Supportive therapy (such as transfusions for low blood counts, medications for pain, antibiotics for infections or hospice care).
- 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. If you decide not to get more treatment, your disease will get worse.

b. Can you participate in other research studies at the same time?

Please check with your study doctor before agreeing to take part in any other research.

c. Other medications, vitamins, and supplements (While in this study, you may not be able to take some or all of the medications or treatments you have been taking for your condition or for other reasons. It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture, or other alternative treatments.

Tell your study doctor about any changes to these during your participation in the research study. Your study doctor will explain to you which treatments or medications need to be stopped for the time you are involved in the research study.

9. How much will it cost you to take part in this study?

If you have health care coverage, we will bill your health care insurer for all standard of care services, tests, and procedures, as applicable. Billing your health care insurer impacts your annual deductible and life-time maximum, if any. This may affect your health care coverage to some extent if you go to another health care provider or institution in the future.

At St. Jude, you will not be responsible for or receive bills for co-pays, co-insurance, deductibles, or similar patient-liability amounts, or for the cost of medical care related to your disease or this study not covered by your health insurer. This includes research-only costs. Research-only tests and procedures (such as optional biopsy or blood samples for biomarker testing) will not be billed to you or your health care insurer.

10. Will you be paid for your time or expenses while taking part in this study?

You will not be paid to take part in this study. Also, your samples and/or 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.

11. What if there is a problem while taking part in this study?

If you are injured from being in this research study, please notify your St. Jude Doctor or the study doctor, **Dr. Brandon Triplett, at 901-595-3300 immediately**. St. Jude will offer you reasonable and necessary medical treatment for that injury. If you need more care than St. Jude can provide or if you prefer to seek treatment elsewhere, we will help you find medical care somewhere else. St. Jude may bill your insurance company or other third parties, if appropriate.

It is not the hospital's policy to provide payment for other types of costs, such as lost wages, disability, or discomfort if you are injured from being in this study. You are not giving up any of your rights by signing this consent form.

12. How will new findings related to your participation in this study be shared with you?

The researcher will tell you of any new information learned during your study participation which might cause you to change your mind about continuing the study. You have the right to learn about the results of the study. If you are interested in learning more about when and how to get the results of this research study, you may contact Dr. Brandon Triplett at 901-595-3300.

13. How will you find out the results of this study?

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
- A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by the 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.

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.

14. Will any genetic tests be done and what are the risks of genetic testing?

As discussed above, we will also obtain samples of your immune cells and other cells during this study. Research performed on your immune cells, and other tissues obtained during this study will include some genetic testing. Genetic testing on material obtained from these samples should help us learn how your immune cells work, and ways to improve transplant therapies in the future.

These additional genetic tests are required and considered research only tests. Results are not reported to you or placed in your electronic medical records. The genetic tests include a partial analysis of genetic material obtained from the samples, and may include whole genome sequencing of cells from your body. No direct benefits to participants are expected from these genetic tests.19Because this genetic testing is being done in a research-only lab, you will not receive the results and a copy will not be placed into your electronic medical record.

Risks of Germline Genetic/Genomic Testing

There may be risks to your privacy and the privacy of your relatives from storing your information in a database. Although measures are taken to protect your privacy, we do not know how likely it is that your identity could become re-connected with your genetic and health information, and confidentiality cannot be guaranteed. If your genetic information were re-identified, personal information about you, your health, and your risk of disease could become known to others, and potentially be used to discriminate against or stigmatize you, your family, or your groups. This could also present unknown risks. We believe the chance that this will happen is very small, but we cannot make guarantees. Your privacy and the confidentiality of your data are very important to us; we will make every effort to protect them.

There is a chance that the genomic test results of your normal tissue will show that you have an inherited health condition, or a condition that can be passed down to any children you have. The

condition discovered might show that you and possibly other family members are at risk of developing tumors or at risk of developing other health problems unrelated to cancer. It is also possible that testing your normal tissue sample will not find any genetic changes that will affect your current management or future health risks. Sometimes, genetic testing can find gene changes that we do not completely understand. This uncertainty may lead to anxiety or confusion.

After learning your results, you might feel anxious, upset or frustrated. Your doctor will discuss these concerns with you and arrange for needed follow-up, such as with the Genetics Service or other support services (social work, spiritual care, or psychology).

As opposed to a research genomic test, any clinical genomic test report comes from a CLIA certified laboratory and the results will be placed into your electronic medical record and may be seen by you, your care team, and other doctors and health care workers at St. Jude or other facilities that obtain your medical record with your permission or legal authority.

Currently, the U.S. law known as the "Genetic Information Nondiscrimination Act" (GINA) prohibits discrimination based on genetic findings in some circumstances:

a. GINA prohibits health care insurers from requesting or requiring genetic information of an individual or an individual's family members or using genetic information for decisions about health insurance coverage or rates, or to exclude preexisting conditions.
b. In companies of 15 or more employees, GINA prohibits employment and employee-related decisions from being made on the basis of genetic information of an individual or an individual's family members.

GINA protections do not apply to:

a. the presence of disease or a health disorder,
b. life insurance, long-term care insurance, or disability insurance. These insurance companies consider may this information in making insurance decisions affecting you,
c. both health care plans and employment from companies employing fewer than 15 people, and
d. people in the military.
e. There are other health plans that GINA does not apply. Please ask your study doctor if you have any questions.

15. What about identifiable private information and identifiable biospecimens (blood, tissue, urine, cells, and any type of data and/or samples) obtained from you during the study?

If you choose to take part in this study, your data and/or specimens will be used to answer the research question(s) and to publish the findings of this study. 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. You will not own your research data and/or specimens. If researchers use your data and/or specimens to create a new product or idea, including those that may have commercial value, you will not benefit financially. There is no plan to share any money with you.

St. Jude's researchers and their collaborators will store the data and specimens collected in this study in electronic databases and other locations and will store specimens in the biorepository or other locations. They may use the data and/or specimens collected in this study for future research purposes and may share some of the data or specimens with others without seeking further consent from you. You may not receive results from that future research.

Sharing data and/or specimens is part of research. It may increase what can be learned from this study and future studies. Often data sharing is required as a condition of funding or for publishing study results. It is also needed to allow other researchers to validate study findings and to come up with new ideas.

Your data and/or specimens may be shared with government agencies, research collaborators, and other researchers and organizations conducting research that may not be related to this study. Your data may also be put in government or other databases/repositories as mentioned in the section above.

Future research using your samples and data is likely to include studies that look at genomic and genetic information to understand causes and cures for health conditions. Because science constantly advances, we do not yet know what other future uses of research data and/or specimens may include. There is no time-limit on sharing of information.

This future research may be unrelated to the current study and may include outside researchers and organizations from around the world. These organizations may include for-profit companies conducting medical research. We or others who distribute data or samples may be paid for data or samples, including yours. You will not receive payment if this happens.

St. Jude will do its best to protect and maintain your data and/or specimens in a safe way. One of the ways we protect your data and/or specimens is by limiting the uses of the information and the type of information that is shared, especially your personal information. This may occur through data sharing agreements and review by oversight groups within St Jude. Often the data and specimens may be coded to protect your identity before they are shared, and we will keep the key to the code in a secure way.

If data and/or specimens are used or shared with any information that may be likely to identify you, such as your name, address, or medical record number, further institutional review and approval would be required. In these cases, we will review whether additional consent from you is required.

Generally, if your data and/or specimens are used and shared without any personal identifiers or only with information that is less likely to identify you (such as the date of a procedure), further review and approval is not needed, and you will not be contacted.

Data sharing could change over time and may continue after the study ends.

The use and sharing of your data and/or specimens is required for participation in this research study. The purpose of research is to learn and discover new information to make improvements to patient care

and/or treatments. To make these improvements, research results must be shared with others. By agreeing to take part in research studies, you are agreeing for your information or data to be used and shared with others. If you are generally not comfortable with the use and sharing of your data and/or specimens in future research as explained this consent, you should talk with your doctor before agreeing to take part in this study.

16. What about permission to use your data/information (HIPAA Privacy Rule), privacy and confidentiality?

Permission to Use Your Data/Information- HIPAA Privacy Rule and Privacy

The HIPAA Privacy Rule defines the situations in which PHI (protected health information) may be used or given to someone outside of the hospital to be used or released for research and other purposes. PHI includes information such as your name, MRN, date of birth, or other identifying information, including research information placed in your medical record.

To do this research, St. Jude Children's Research Hospital (St. Jude) will need to collect, use, and share your private health information. St. Jude is required by law to protect your health information. By signing this consent form, you give St. Jude permission to use and/or release (share) your private health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

If you sign this consent form, you give permission to all researchers and their staff involved in the study at St. Jude to use or release (share) your health information that identifies you for the research study described in this document.

The health information that we may use or release includes things learned from the procedures and treatments describes in this consent form, as well as all information from your medical record (which may include information such as HIV status, drug, alcohol, or STD treatment, genetic test results, or mental health condition and/or treatment, physical examinations, and lab tests).

If you sign this consent form, you give St. Jude permission to share your information for future research studies about disease or advancing science and for future unspecified research. You also give permission for us to place this information on databases as described below under Privacy and Confidentiality.

Information from research testing will be analyzed in a CLIA-certified (medical) laboratory or a research-only laboratory. By signing, you give St. Jude permission to put your research information obtained from a CLIA-certified laboratory into your medical record. Results from research-only laboratories will not be put into your medical record and will not generally be available to you or your doctor.

If you sign this document, you give St. Jude permission to share your information for future research studies and for the placement of information in databases as described in #14 of this consent form. By signing, you will also give St. Jude permission to put your research information, including testing,

imaging, genomic and genetic information, other information and studies, and other sensitive information in your medical record (unless the research information is from a research-only laboratory). Any information placed in the medical record becomes a permanent part of your record, is kept indefinitely, and is not protected by a Certificate of Confidentiality (Certificate of Confidentiality, if included with this study, is described below under Privacy and Confidentiality). It is protected like any other part of your medical record as described in the Notice of Privacy Practices. You have the right to see, copy, and ask for changes to your PHI that will be used or shared. However, research information may not be available until after the end of the study.

When you first registered at St. Jude, you received a copy of the St. Jude Notice of Privacy Practices. It tells how your PHI, including research information placed in your medical record, may be used or given to someone outside of St. Jude. You have the right to read the Notice of Privacy Practices before you sign this consent form. It may have changes 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

A decision to take part in this research means that you agree to let the research team use and share your PHI with other researchers for purposes of 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.

Federal agencies such as the Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), the National Institutes of Health (NIH), and St. Jude Children's Research Hospital Institutional Review Board (IRB), your insurance company and other health benefits plan (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.

Information about you may also be shared with representatives from the Miltenyi Biotec Corporation, the manufacturer of the investigational CliniMACS blood cell selection device. This information will include any information related to how well the device works, if there is a malfunction and any related problems that you may experience as a result of the malfunction of the device.

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 a worldwide research organization of scientists and doctors who study important issues in transplantation.

Your donor blood 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 for monitoring the clinical and laboratory activities of institutions that provide research and treatment with certain blood cell products including blood progenitor 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.

Because this information may be linked to you, absolute privacy cannot be guaranteed.

By signing this consent form, you are allowing your data and/or biological sample 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).
- 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.
- Other committees or people involved in overseeing research studies.
- Miltenyi Biotec, the maker of the CliniMACS device system

The people who may view, request, receive, or use your private health information include St. Jude researchers and their staff, and other doctors, nurses, and staff members. Additionally, St. Jude may share your information with other people or groups of people. These include:

- Transplant related oversight agencies or registries that may receive and process PHI (CIBMTR, FACT and NMDP); and/or
- St. Jude Institutional Review Board and St. Jude Institutional Biosafety Committee

You do not have to sign this consent form which gives your permission, but if you do not, you may not receive research-related treatment.

Please note that you may change your mind and take back (revoke) this permission at any time. Even if you take back this permission, St. Jude Children's Research Hospital may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To take back this consent form/permission, you must write to:

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

This permission does not have an expiration date.

Confidentiality

We will protect the confidentiality of your information to the extent reasonably possible.

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.

If you consent to take part in this study, all information learned from the study will be stored, maintained, and protected on password protected computer systems that are on secure servers and stored within locked cabinets and offices accessible only to the study team. Your study results will be kept in your research records for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will also be kept for an unknown length of time.

Research data obtained from this study from standard of care tests and procedures and research tests and procedures such as tumor and normal specimens and genetic data, are often shared with the research community using various databases, including those maintained by St. Jude, the federal government, and international collaborative databases. This is to advance scientific discovery, and to satisfy requirements of organizations that fund research, and journals that publish the results of research.

There are two types of databases used for sharing research data. One is a public, unrestricted access database and the other is a controlled access database. Each is described below.

Unrestricted access databases:

The information from research studies using your samples, genetic information, and some health information may be freely available in a public, unrestricted database that anyone can use. A public database could include information on hundreds of thousands of genetic variations in your DNA code, as well as your ethnic group and sex. Summary-level information about all participants included in a dataset, including you, but not genetic data for each individual, may be shared.

Some examples of information that may be shared includes how different genes are associated with different traits or diseases across the many participants in the dataset, or how often certain gene changes are seen across participants from many studies. However, the risk of anyone identifying you with this information is very low. This public information will not be labeled with your name or other information that could be used to easily identify you.

You will not be notified every time your genomic information is used for research. We also do not know what types of future research will be done with genomic data from this study.

Controlled access databases:

Your individual genomic data and health information may be put in a controlled-access database. This means that only researchers who apply for and get permission to use the information for a specific research project will be able to access the information. Your genomic data and health information will not be labeled with your name or other information that could be used to easily identify you.

Researchers approved to access information in the database must agree to protect the information and not to try to identify you. Examples are the St Jude Cloud, which is run by St. Jude, the database of Genotypes and Phenotypes which is run by the Federal Government, and the European Genome-Phenome archive. These are databases available to researchers to use genomic information from tumor and non-tumor samples to study genetic changes in pediatric diseases.

If you decide you would like to take part in this research study, please ask any questions you have, and read and sign this consent form. You will be given a copy of it to keep. A copy of this consent form will also be put in your patient notes, one will be put with the study records, and one may be sent to the Research Sponsor.

You can have more time to think this over if you are at all unsure.

Thank you for taking the time to read this informed consent document and to consider taking part in this study.

17. Optional Research Tests or Procedures

This section is about optional research studies you can choose to take part in if you participate in the main research study.

You will not get health benefits from any of these optional studies. There are no costs to you or your insurance or other payors. You will not be paid for taking part in these optional studies. If any of the research leads to new tests, drugs, or other commercial products, there is no plan to share any money with you.

Optional ATG PK Research Test

This research test is optional. You may choose not to undergo this optional testing and can still take part in this study. The purpose of this optional research test is to evaluate drug exposure and to determine the length of time that ATG remains active following HCT in recipient participants of this study through pharmacokinetic (PK) testing. There is a designated area with checkboxes at the end of this consent form to mark whether you agree to take part in this voluntary study.

Below is a diagram that gives an overview of this optional test.

Optional Research Test to be collected on this study	Blood volume total for length of study	Frequency of sample collection during this study
ATG PK	About 3 teaspoons	Pre and Post-3rd dose on Day -10, Once each on Days -8, -7, -5, -3, 0, +7, +14

By signing this consent form, you are voluntarily and freely donating your blood samples to St. Jude Children's Research Hospital and hereby relinquish all property rights, title, and interest you may have in this sample.

The researchers leading the optional studies believe the results will help other people with cancer, HIV, sickle cell disease and other health problems in the future.

The results from these optional research studies will not be added to your medical record nor will you know the results.

You can still take part in the main study even if you say "no" to the optional study. If you sign up for but cannot complete any of the optional study for any reason, you can still take part in the main study. If you choose to take part in these studies later, you will be asked to sign a consent form.

What will happen in this Optional Study)?

If you agree to take part in this optional study, here is what will happen next:

Test/Procedure	Time Point	Purpose
ATG PK Researchers at St. Jude will perform research tests on blood.	Nine total tubes of blood (3 teaspoons or about 18mL) would be taken Pre and Post-3rd dose on Day -10, Once each on Days -8, -7, -5, -3, 0, +7 and +14.	• To evaluate drug exposure and to determine the length of time that ATG remains active following HCT.
Please initial and date your choice: I agree to have my blood used for ATG PK optional research study		**YES: _____ __/ ___/ ___** **Initials Date** **NO: _____ ___/___/___** **Initials Date**

What if I Change my Mind?

If you decide you no longer want your samples to be used, you can call the study doctor, Dr. Brandon Triplett at 901-595-3300,) who will let the researchers know. Then, any sample that remains in the bank will no longer be used. Samples or related information that have already been given to or used by researchers will not be returned or removed.

18. Signatures

PARENT/Legal GUARDIAN STATEMENT (Required for participants younger than 18 years)

I have read this consent form or it was read to me. I have been encouraged to ask questions and all my questions have been answered. I give my 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 7-17 years old)

□ The research was explained to the minor participant aged 7 to 13 years in age-appropriate terms and the minor verbally agreed to take part in the study.

□ Minor Age 14 to 17 years old Assent Signature:

I have read this consent form or it was read to me and discussed in a way that I could understand. I have been encouraged to ask questions and all of my questions were answered. I agree to take part in this research study.

_____ _____ _____AM/PM

Minor Assent Signature Date Time (circle one)

□ 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 STATEMENT (Age 18 years and older):

I have read this consent form or it was read to me. I have been encouraged to ask questions and all of 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 consent form has been given to the participant or his/her representative.

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

_____

Researcher/Designee 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 Signature	Date	Time	(circle one)
_____	_____	_____AM/PM	
Interpreter (if needed) Signature	Date	Time	(circle one)

PLEASE UPLOAD COMPLETED CONSENT FORM TO EPIC.

Initial version dated: 03/01/2024
Consent document date: 03/01/2024