Informed Consent Coversheet

Official Study Title	**T-CELL RECEPTOR (TCR) ALPHA BETA+/CD19+ DEPLETION IN HAPLOIDENTICAL ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION (ALLO-HCT) FOR ADULT AND PEDIATRIC PATIENTS WITH HEMATOLOGICAL MALIGNANCIES AND NON-MALIGNANT DISORDERS (HAPLOTAB)**
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H-50045- HAPLOTAB: T-CELL RECEPTOR (TCR) ALPHA BETA+/CD19+ DEPLETION IN HAPLOIDENTICAL ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION (ALLO-HCT) FOR ADULT AND PEDIATRIC PATIENTS WITH HEMATOLOGICAL MALIGNANCIES AND NON-MALIGNANT DISORDERS

Concise and Focused Presentation

* We ask you to take part in a research study because treatment of your disease requires you to receive a stem cell transplant.
* We want to see if specially treating the donor's blood cells used for the stem cell transplant can minimize or prevent graft versus host disease (GVHD).
* Your doctors will follow you after your transplant.
* The study will last approximately one year. You will visit the clinic over a several month period during the study. For purposes of the study, we will collect health-related information for a year from the time of stem cell transplant.

* The study has possible risks:
- These cells might attack other parts of your body and cause graft versus host disease (GVHD)
- You may have trouble receiving the stem cell infusion
- The T cells may not engraft and you may need an additional stem cell transplant
- The T cells may not completely engraft and you may need additional donor cells or may need to enter another program to treat your condition.
- Risk of Post-Transplant Lymphoproliferative Disease (PTLD)
- Increased risk of infection
- A loss of confidentiality

We may not know all the risks.

* Potential benefits:
- The potential for cure or improved survival
- Decrease risk of developing GVHD

This research study is voluntary. You may choose not to take part in this study.

Background

You are invited to take part in a research study. Please read this information and feel free to ask any questions before you agree to take part in the study. In this document, the term "you" refers to either you or your child. You are being asked to participate in this study because treatment of your disease requires you to receive a stem cell transplant.

Stem cells or "mother" cells are the source of normal blood cells and lead to recovery of blood counts after bone marrow transplantation. Unfortunately, there is not a perfectly matched stem cell donor (like a sister or brother) and your disease does not permit enough time to identify another donor (like someone from a registry list that is not your relative) or we have not identified another suitable donor. We have, however, identified a close relative of yours whose stem cells are not a perfect match, but can be used. It may be necessary to isolate stem cells from a haploidentical (half-match) donor in order to provide bone marrow function. Because the stem cells from the donor are only half-matched to you, there is an increased risk of developing graft-versus-host disease (GVHD) and other immune-mediated

complications, and there may also be a longer delay in the recovery of your new immune system. Seventy to ninety percent (70-90%) of the people who receive unchanged bone marrow or stem cells from this type of donor will develop moderate to severe GVHD.

GVHD is a serious and sometimes fatal side effect of stem cell transplant. GVHD occurs when the new donor cells (graft) recognize that the body tissues of the patient (host) are different from those of the donor and attacks them. The organs usually involved in GVHD are skin, liver, and intestines. GVHD may cause severe rashes, diarrhea, liver disease, and even death. GVHD is caused by a type of immune cell in graft called T cells. Because there is a high chance for GVHD with the type of transplant you will receive, most of the T cells that cause GVHD will be removed from your donor graft in a process called "T-cell receptor alpha beta depletion". While T cells can cause GVHD, they are also the part of the immune system that help fight infections. Hence, even though the T cell depletion procedure can reduce the risk of GVHD it may also result in slower recovery of your immune system and make you vulnerable to serious infections after transplant.

This research study is sponsored by Baylor College of Medicine.

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

Purpose

In an effort to lower the occurrences and severity of graft -versus-host disease (GVHD) in patients and to lower the rate of transplant failure, we would like to specially treat the donor's blood cells to minimize the cells that are most likely to attack your tissues.

Procedures

The research will be conducted at the following location(s):
Baylor College of Medicine, TCH: Texas Children's Hospital, and TMH: The Methodist Hospital.

A total of 47 subjects will be asked to participate in this study. Your participation in the project will last approximately one year with follow-up exams.

To participate in this study, you will need to have a central line (a thin plastic catheter or tube that is placed during surgery, into one of the large veins in the neck or chest). Central lines are used to give intravenous medications (goes directly into the vein) or to take blood samples without you having to endure frequent needle sticks. Also, before treatment can begin, we will test your blood for viruses which can cause problems after the transplant. These viruses include Hepatitis B (which causes liver damage), cytomegalovirus (which causes lung disease) and HIV (which causes AIDS, an immune system disorder). If you are positive for HIV, we will not be able to continue with the transplant. If you are a female of childbearing potential, we will also perform a pregnancy test. If you are pregnant, we will not be able to continue with the transplant due to the possible effects on the fetus.

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Hematopoietic Cell Transplant (HCT):

Hematopoietic cell transplant (HCT) is a technical term for a blood stem cell transplant- a medical procedure used to treat people with a variety of life-threatening disease. You may also hear the procedure referred to as: bone marrow transplant, stem cell transplant (or peripheral blood stem cell transplant).

Blood stem cells (hematopoietic stem cells) are special cells that enable one's body to produce:
- White blood cells, that are needed to fight infections
- Red blood cells, that carry oxygen to, and remove waste from, our body's cells
- Platelets, that help blood clot

Blood stem cells live in the bone marrow --the spongy tissue inside our bones

Conditioning Regimen:
To prepare your body for transplantation, you will be given chemotherapy and possibly radiation, which is called the conditioning regimen or preparative regimen. It is standard to give a conditioning regimen (such as chemotherapy) before a bone marrow transplantation. The conditioning regimen helps prepare your body to accept the donor cells. The treatment plan for the conditioning regimen and prevention of GVHD (using anti-thymocyte globulin, ATG) will be discussed with you in a separate consent form which you will also sign.

In order to prevent a complication called Post-Transplant Lymphoproliferative Disorders (PTLD), the conditioning regimen will also include a medication called Rituximab, which will be given on day -1 (the day before the infusion of the stem cell product), at a dose of 200 mg/m2 for one dose. This dose was selected based on several published studies documenting safety and efficacy of this dose in the context of stem cell transplantation using T-cell receptor alpha/beta depletion.

Donor Stem Cell Transplant:
Before treatment can begin, stem cells will be collected from the donor who has been selected as the best match for you. The donor stem cells will be run through a machine that removes most of the alpha-beta (alpha beta+) T cells and most of the B cells and leaves the stem cells (called CD34+ cells). Accordingly, the stem cell product developed using this procedure, and used as the hematopoietic (blood) cell transplant source on this study, is considered an investigational product.

There is some evidence to suggest that the use of a fresh stem cell product results in a better outcome following the stem cell infusion. Every effort will be made to give you a fresh stem cell product; however, a frozen product may be infused when necessary and you will be told were this to be necessary. On the day of the transplant (called Day 0) you will be given the alpha beta+ T cell depleted CD34+ stem cells through your central venous catheter. You may need more than one infusion of stem cells to reach the

goal number of CD34+ stem cells. In this case, your donor will be collected again (usually 1-2 days later) and the product will undergo a selection of CD34+ stem cells without performing an additional alpha beta T-cell depletion procedure. Once in your body, the CD34+ stem cells have the ability to grow into new blood cells and immune cells. This will happen over a several months period of time after the transplant.

For purposes of the study, we will collect health-related information for a year from the time of stem cell infusion. We will be determining survival, relapse, infections and GVHD that may occur following transplant.

Clinically Relevant Research Results

The main benefit you may gain from participating in this research study is the potential for cure of your underlying disease. Participating in this research protocol can potentially decrease the risk of developing graft versus host disease (GVHD) compared to standard of care approach for hematopoietic cell transplant.

Sharing and Future Research Studies with Identifiable Private Information

Information that identifies you may be removed from your identifiable private information collected as part of this research, and after such removal, your information may be used for future research studies or distributed to another investigator for future research studies without additional consent/authorization from you.

Research related health information

Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you sign this document, you give permission to people who give medical care and ensure quality from Baylor College of Medicine, TCH: Texas Children's Hospital, and TMH: The Methodist Hospital to use or disclose (release) 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:

- Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
- Specific information concerning HIV
- Demographic information (name, D.O.B., age, gender, race, etc.)
- Billing or financial records

The health information listed above may be used by and or disclosed (released) to researchers, their staff and their collaborators on this research project, the Institutional Review Board, Baylor College of Medicine, TCH: Texas Children's Hospital, and TMH: The Methodist Hospital.

Agents of the U.S. Food and Drug Administration may inspect the research records including your health information. Agents of regulatory agencies such as the U.S. Department of Health and Human Services will be permitted to inspect the research records including your health information.

A Data and Safety Monitoring Board will have access to the research records including your health information.

Use or Disclosure Required by Law

Your health information will be used or disclosed when required by law.

Your health information may be shared with a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury, or disability and conducting public health surveillance, investigations or interventions.

Baylor College of Medicine, TCH: Texas Children's Hospital, and TMH: The Methodist Hospital are required by law to protect your health information. By signing this document, you authorize Baylor College of Medicine, TCH: Texas Children's Hospital, and TMH: The Methodist Hospital to use and/or disclose (release) your 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.

Please note that the research involves treatment. You do not have to sign this Authorization, but if you do not, you may not receive research-related treatment. To maintain the integrity of this research study, you generally will not have access to your personal health information related to this research until the study is complete. However, your health information that is necessary to your care will be provided to you or your physician. At the conclusion of the research and at your request, you generally will have access to your health information that Baylor College of Medicine, TCH: Texas Children's Hospital, and TMH: The Methodist Hospital maintain in a designated record set, which means a set of data that includes medical information or billing records used in whole or in part by your doctors or other health care providers at Baylor College of Medicine, TCH: Texas Children's Hospital, and TMH: The Methodist Hospital to make decisions about individuals. Access to your health information in a designated record set is described in the Notice of Privacy Practices provided to you by representatives of the specific institution where you are being enrolled into this research study which are: Baylor College of Medicine, TCH: Texas Children's Hospital, and TMH: The Methodist Hospital.

Please note that you may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, researchers, their staff and their collaborators on this research project, the Institutional Review Board, regulatory agencies such as the U.S. Department of Health and Human Services, FDA, Baylor College of Medicine, Data and Safety Monitoring Board, TCH: Texas Children's Hospital, and TMH: The Methodist 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. If you revoke this Authorization, you may no longer be allowed to participate in the research described in this Authorization.

To revoke this Authorization, you must write to: Erin Morales, MD
1102 Bates Street
Feigin Tower, Suite 1770
Houston, TX 77030

This authorization does not have an expiration date. If all information that does or can identify you is removed from your health information, the remaining information will no longer be subject to this authorization and may be used or disclosed for other purposes.

No publication or public presentation about the research described above will reveal your identity without another authorization from you.

Potential Risks and Discomforts

The major risk is that your bone marrow may recover more slowly than it would with a standard bone marrow transplant. This might increase the risk of infection and bleeding. It is possible that the marrow will not recover at all. In that case, you may need another stem cell transplant.

Graft-versus-host disease (GVHD): GVHD occurs when the new stem cells (graft) recognize that the body tissues of the patient (host) are different from those of the donor. Signs of GVHD include diarrhea, skin rashes and blisters, and liver problems. GVHD can be dangerous or even fatal and requires drug treatment. If this disease does not go away within a few months, it may change into a long-term form (chronic) that involves the lungs, eyes, mouth, liver, skin, joints, or muscles.

Stem Cell Infusion: Side effects may include blockage of the blood vessels in the lungs, kidney damage, trouble breathing, failure of marrow to grow and make normal blood cells and development of GVHD.

Non-engraftment: This means that the stem cells given to you from the donor have not started to grow in your bone marrow and are not working to produce new blood cells. This may happen if the pre-conditioning chemotherapy did not do its job of preparing your body so that it is ready for the donor stem cells. If this happens, you will be at increased risk for complications such as infection (from not having enough white blood cells), bleeding (from not having enough platelets) and difficulty breathing (from not having enough red blood cells to carry oxygen around the body). If no further treatment is received, it is possible that you may die. If non-engraftment occurs, you may need another stem cell transplant.

Incomplete Engraftment: Even if engraftment occurs, it may be incomplete. This is frequently seen after other transplant treatment plans. Because of this, all patients will be monitored for engraftment at regular time points after transplant. Again, if incomplete engraftment occurs, you will be given the option of

receiving additional donor stem cells or of entering into other programs to treat this condition.

Central Line: The risks of having a central line are similar to the risk of the surgical procedures to insert the catheter. These risks include a pneumothorax (air inside the chest), bleeding, infection, and the risks associated with receiving anesthesia. These risks will be explained in greater detail by your surgeon prior to placement of the central line. After placement, the central line may become infected requiring hospitalization, treatment with intravenous (IV) antibiotics (medicines given directly into the bloodstream through a vein), and possibly removal of the line and placement of a new line. In addition, a blood clot may develop in the line. If the clot cannot be dissolved, the line will need to be replaced and a new line inserted.

Additional Risks: Stem cell transplant patients have an increased risk of infections, especially those due to cytomegalovirus (CMV), herpes simplex virus (HSV), Epstein-Barr virus (EBV) causes glandular fever or mono, the kissing disease, pneumonia, and other viruses. CMV, HSV, and EBV are all common viruses people may get but can cause serious infections in patients with suppressed immune systems. Preventative medicines are given when possible and treatment is started very promptly, usually before the infection is confirmed. The administration of blood products carries the risk of blood born infections such as hepatitis, CMV, and HIV. Blood products are carefully screened for these agents. Other complications of an unexpected nature may occur. In fact, almost every patient presents with some new or very rare complication during his/her transplant.

Post-Transplant Lymphoproliferative Disorders (PTLD): a group of potentially life-threatening conditions that affect patients who have had a stem cell transplant. PTLD occurs when the immune system is weakened after transplant, making it not very effective at removing certain viral infections such as the Epstein-Barr virus (EBV); it also is not always effective at monitoring for pre-cancer or cancer cells that may develop from long-term exposure to EBV. These abnormal cells often grow and can spread to other parts of the body. A single dose of Rituximab given i.v. on Day -1, will aim to minimize the risk of developing PTLD.
Rituximab toxicity includes but not limited to: Hypersensitivity reactions (for which premedication with acetaminophen and diphenhydramine will be administered). The most common toxicities are infusion-related and may include fever, chills, headache, nausea, vomiting, swelling under the skin (13%), hypotension (10%), bronchospasm (8%) and arrhythmias.

Study staff will update you in a timely way on any new information that may affect your decision to stay in the study. There is a small risk for the loss of confidentiality. However, the study personnel will make every effort to minimize these risks.

Potential Benefits
The benefits of participating in this study may be: The potential for cure or improved survival. Potentially, participation in this protocol will decrease the risk of developing GVHD. This research may benefit society as a whole by assisting in the development of better treatments for patients with leukemia or

other hematopoietic or immunological disorders. However, you may receive no benefit from participating.

Alternatives

The following alternative procedures or treatments are available if you choose not to participate in this study: You would still be able to receive treatment with hematopoietic cell transplant using the standard care approach.

Subject Costs and Payments

All medical expenses related to this treatment protocol will be the responsibility of the patient. You will have an opportunity to discuss the expenses or costs associated with participation in this study. All costs related to your medical care will be charged to you or your insurance carrier. You and/or your insurance will be charged for the cost of using the machine for stem cell selection discussed in the Procedures section. The cost of the using machine (designed to select stem cells) is anticipated to be similar to the cost of the previously used FDA approved machine, which is no longer available. The cost will be included in the overall cost of the stem cell transplant. We anticipate that the cost will be covered by insurance as with the standard machine. The overall cost of the stem cell transplant will be discussed with your insurance carrier, or other agencies as needed. Financial counseling is available upon request to discuss the cost of this treatment and your insurance coverage, or coverage as provided by other agencies.

You will not be paid for taking part in this study.

Research Related Injury

If you are injured as part of your participation in this study, there are no plans to pay you.

Research personnel will try to reduce, control, and treat any complications from this research. If you are injured because of this study, you will receive medical care that you or your insurance will have to pay for just like any other medical care.

Women of Childbearing Potential

It is possible that the medicines used in this study could injure a fetus if you or your partner becomes pregnant while taking them. Because of the potential risks involved, you or your partner should not become pregnant while you are participating in this study.

If you are sexually active or become sexually active and can get pregnant or can get your partner pregnant, you must agree to use one of the following forms of birth control every time you have sex:

* oral contraceptives ("the pill"),
* intrauterine devices (IUDs),
* contraceptive implants under the skin, or contraceptive injections,
* condoms with foam.

Should you become pregnant while on this study, you must immediately notify the study personnel.

The investigator will assist you in finding appropriate medical care. The investigator also may ask to be allowed to continue getting information about your pregnancy. You can choose not to provide this information.

Subject's Rights

Your signature on this consent form means that you have received the information about this study and that you agree to volunteer for this research study.

You will be given a copy of this signed form to keep. You are not giving up any of your rights by signing this form. Even after you have signed this form, you may change your mind at any time. Please contact the study staff if you decide to stop taking part in this study.

If you choose not to take part in the research or if you decide to stop taking part later, your benefits and services will stay the same as before this study was discussed with you. You will not lose these benefits, services, or rights.

The investigator, ERIN MORALES UBICO, and/or someone he/she appoints in his/her place will try to answer all of your questions. If you have questions or concerns at any time, or if you need to report an injury related to the research, you may speak with a member of the study staff: ERIN MORALES at (832) 826-0860 during the day and after hours.

Members of the Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals (IRB) can also answer your questions and concerns about your rights as a research subject. The IRB office number is (713) 798-6970. Call the IRB office if you would like to speak to a person independent of the investigator and research staff for complaints about the research, if you cannot reach the research staff, or if you wish to talk to someone other than the research staff.

The National Institutes of Health (NIH) and the National Cancer Institute (NCI) may have access to your

records for research purposes. Coded information may be provided to the NIH/NCI such as your Patient ID, your Zip code, your country and your birth date (month and year). However, in the event of an audit, the NIH/NCI might have access to more information that is part of your research record.

If your child is the one invited to take part in this study you are signing to give your permission. Each child may agree to take part in a study at his or her own level of understanding. When you sign this you also note that your child understands and agrees to take part in this study according to his or her understanding.

Please print your child's name here _____

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Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

Subject	Date
Legally Authorized Representative Parent or Guardian	Date
Investigator or Designee Obtaining Consent	Date
Witness (if applicable)	Date
Translator (if applicable)	Date