MAIN STUDY CONSENT

Study Title: Safety and efficacy of Miltenyi CliniMACS® CD34 Reagent System for transplant protocol utilizing haploidentical CD34+ selected cells combined with single unit umbilical cord blood transplant for treatment of high-risk hematologic disorders

Principal Investigator: Jonathan Gutman, MD
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You are being asked to be in a research study. This form provides you with information about the study. A member of the research team will describe this study to you and answer all of your questions. Please read the information below and ask questions about anything you don't understand before deciding whether or not to take part.

Why is this study being done?

Transplantation with cord blood is a standard therapy in many transplant hospitals around the world. Previous experience with cord blood stem cell transplantation has led to extended disease-free survival or cure for some patients.

One disadvantage of cord blood transplantation is that it takes longer for blood counts to recover in patients treated with cord blood compared to patients who receive other types of transplant. Studies have shown that this is because of the small number of cells in one bag of cord blood. One way to give a patient more cells is to combine the cord blood with stem cells from a family member who is not a perfect match, that is called a haploidentical donor. Haploidentical means that the cells have the same genetic information in some, but not all chromosomes.

The study requires stem cell selection using a device called the Miltenyi CliniMACS® CD34 Reagent System. The device is not FDA approved for this specific indication of use. Therefore, the process of isolating the haploidentical stem cells is "investigational." "Investigational" means that the use of this device has not been approved by the U.S. Food and Drug Administration (FDA).

This research study plans to learn more about this treatment of high-risk hematologic disorders with haploidentical stem cells combined with umbilical cord blood (UCB) transplant. These isolated stem cells may be referred to as the "study product" during this consent.

The study Investigators have designed this research study to evaluate if the enrichment with stem cells using the Miltenyi CliniMACS® CD34 Reagent system is a safe and efficacy treatment for your high-risk hematologic disorder. The study Investigators will review your test results and overall response to the study product to help determine the safety and

efficacy of the transplanted study product. We do not guarantee or promise that the treatment or procedures described in this study will be effective in treating your medical condition.

You are being asked to take part in this study because you have a high-risk hematologic disorder that may be treatable with a blood stem cell transplant and you do not have a histocompatible blood stem cell (also called perfect match) donor.

The Investigators of this study want you to understand that subjects in clinical trials include only those who are completely informed and choose to participate. Please take your time to make your decision whether to participate. We encourage you to discuss your decision with your doctor, family and friends.

Other people in this study

Up to 200 people from your area will participate in the study.

What happens if I join this study?

SCREENING PERIOD

Before you are allowed to join the study, your study doctor will examine you and take some tests. These tests are being done as part of standard of care, as any patient who receives bone marrow transplant, and would be done even if you did not participate in this study. If you have had any of them recently, your doctor may decide not to repeat them.

TREATMENT PERIOD

You will be treated according to the standard of care treatment plan. You will be admitted to the hospital for the duration of the transplantation process, about 27 days. You will be admitted 7 days prior to transplant and discharged about 20 days after transplant. Your total stay in the hospital will be directed by your study doctor. You may need to stay in the hospital 3 – 6 weeks post-transplant.

During your stay in the hospital you will receive the standard of care tests for a transplant patient.

Stem Cell Transplantation

Prior to your transplantation you will review and sign a separate consent to receive a course of drugs to prepare you for transplant, these drugs are standard of care and are

considered **"standard conditioning"** for stem cell transplantation. All patients undergoing transplantation, whether on a study or not, receive conditioning prior to transplantation.

In addition to the above standard conditioning, you will also receive standard of care pre-medications to help prevent transplant complications of the stem cell transplant.

You will receive single unit, unaltered UCB infusion under standard of care. In addition, the study product will be prepared from donor cells with the use of the Miltenyi device. The study product will be transplanted into you using standard transplant practices.

Post-Transplant

After the stem cell transplant is complete you will receive standard of care support as needed and directed by your study doctor. Your study doctor will oversee your care to watch for any complications that may be related to your transplant or the study product. Your total stay in the hospital will be directed by your study doctor.

FOLLOW-UP PERIOD

After your bone marrow is confirmed as engrafted, , you will go off study and be followed by your medical doctor under standard of care practices.

What are the possible discomforts or risks?

The side effects associated with transplantation will not be different from standard of care transplantation. Because this is a research study, there may be additional side effects which are not known or predictable at this time. The known or possible side effects of the treatments you will receive as part of this study are listed below.

There is a risk that people outside of the research team will see your research information and loss of confidentiality. We will do all that we can to protect your information, but it cannot be guaranteed.

<u>Risks Related to the CliniMACS CD34 Reagent Systems</u>

The results summarized by the Manufacturer, Miltenyi, support that the device to select stem cells is safe for clinical use with human subjects. The device is approved by FDA for other indication. The potential application of the device as an investigational product is broad. Infusion of purified stem cells has been studied in a number of clinical applications after myeloablative or lymphoablative therapy including reduction of tumor cells in the transplant and depletion of T-cells for autologous (autoimmune diseases) and allogeneic

transplantations. Individual risk analysis on the therapeutically used target (stem) cells isolated by this device should be addressed by each site.

Processing and Device Risks
Potential risks to the study product or patient could include:

- Reagent system failure
- Operator error

Specifically, potential risks are 1) failure of Miltenyi CliniMACS® CD34 Reagent System to select CD34+ cells, and/or 2) introduction of a microorganism that may cause an infection, and/or 3) failure of the bone marrow to engraft.

The study may include risks that are unknown at this time.

Risks related to transplant are <u>outlined in the standard of care bone marrow transplant consent</u>.

What are the possible benefits of the study?
This study is designed for the researcher to learn more about stem cell transplantation and hematological disorders involving the blood or bone marrow.

Are there alternative treatments?
There may be other ways of treating your hematologic disorder. These other ways include a standard of care bone marrow transplant, another clinical research trial or you could also choose to get no treatment at all.

You should talk to your doctor about your choices. Make sure you understand all of your choices before you decide to take part in this study. You may leave this study and still have these other choices available to you.

Who is paying for this study?
This is an investigator-initiated study. UCH/ClinImmune will provide the study product (purified haploidentical peripheral blood CD34+ cells (family member stem cells)) to you free of charge for the duration of your study participation.

Will I be paid for being in the study?
You will not be paid to be in the study.

Will I have to pay for anything?
All tests and procedures in this study are considered standard of care; therefore you will need to pay for all tests and procedures. These include the bone marrow transplant, clinic visits and laboratory tests. You may be responsible for co-payments and deductibles that are standard for your insurance coverage.

Ask your study doctor to discuss the costs that will or will not be covered. This discussion should include the costs of treating side effects. Otherwise, you might have unexpected expenses from being in this study.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the Clinical Trials and Insurance Coverage information from this Web site. Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

Is my participation voluntary?
Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you choose to take part, you have the right to stop at any time. If you refuse or decide to withdraw later, you will not lose any benefits or rights to which you are entitled.

If there are any new findings during the study that may affect whether you want to continue to take part, you will be told about them.

Can I be removed from this study?
The study doctor may decide to stop your participation without your permission if the study doctor thinks that being in the study may cause you harm, or for any other reason.

What happens if I am injured or hurt during the study?
If you have an injury while you are in this study, you should call Dr. Jonathan Gutman immediately. His phone number is 720-848-0220.

We will arrange to get you medical care if you have an injury that is caused by this research. However, you or your insurance company will have to pay for that care.

Who do I call if I have questions?
The researcher carrying out this study is Dr. Jonathan Gutman. You may ask any questions you have now. If you have questions later, you may call your study doctor, Dr. Jonathan Gutman at 720-848-0220. You will be given a copy of this form to keep.

You may have questions about your rights as someone in this study. You can call your study coordinator with questions. You can also call the Colorado Multiple Institutional Review Board (COMIRB). You can call them at 303-724-1055.

A description of this clinical trial will be available on http://www.Clinical Trials.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.

Who will see my research information?

The University of Colorado Denver | Anschutz Medical Campus (the University) and its affiliated hospital(s) have rules to protect information about you. Federal and state laws including the Health Insurance Portability and Accountability Act (HIPAA) also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.

The institutions involved in this study include:

- University of Colorado Denver | Anschutz Medical Campus
- University of Colorado Health

We cannot do this study without your permission to see, use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will see, use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside the UCD and its affiliate hospitals may not be covered by this obligation.

We will do everything we can to maintain the confidentiality of your personal information but confidentiality cannot be guaranteed.

The use and disclosure of your information has no time limit. You can cancel your permission to use and disclose your information at any time by writing to the study's Principal Investigator (PI), at the name and address listed below. If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in this study.

Jonathan Gutman, MD
CU Anschutz Medical Campus, Anschutz Cancer Pavilion
1665 Aurora Court, Mail Stop F754
Aurora, CO 80045 United States

Both the research records that identify you and the consent form signed by you may be looked at by others who have a legal right to see that information, such as:

- Federal offices such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP) that protect research subjects like you.
- People at the Colorado Multiple Institutional Review Board (COMIRB)
- The Institutional Review Board that is responsible for overseeing this research

- The study doctor and the rest of the study team.
- Members of your care team that have access to your electronic medical records.
- Officials at the institution where the research is conducted and officials at other institutions involved in this study who are in charge of making sure that we follow all of the rules for research.

We might talk about this research study at meetings. We might also print the results of this research study in relevant journals. But we will always keep the names of the research subjects, like you, private.

You have the right to request access to your personal health information from the Investigator. To ensure proper evaluation of test results, your access to these study results may not be allowed until after the study is completed.

Information about you that will be seen, collected, used and disclosed in this study:

- Name and Demographic Information (age, sex, ethnicity, address, phone number, etc).
- Your social security number
- Portions of your previous and current Medical Records that are relevant to this study, including but not limited to Diagnosis(es), History and Physical, laboratory or tissue studies, radiology studies, procedure results
- Research Visit and Research Test records
- Tissue samples and the data with the samples.
- Billing or financial information

Your care team, including family doctor, may be made aware of your participation in the study through your electronic medical records.

What happens to Data, Blood and Specimens that are collected in this study?

Scientists at the University and the health systems involved in this study work to find the causes and cures of disease. The data, blood and specimens collected from you during this study are important to this study and to future research. If you join this study:

- The data, blood, or other specimens given by you to the investigators for this research no longer belong to you.
- Both the investigators and any sponsor of this research may study your data, blood, or other specimens collected from you.
- If data, blood, or other specimens are in a form that identifies you, UCD or the hospitals involved in this study may use them for future research only with your consent or Institutional Review Board (IRB) approval.
- Any product or idea created by the researchers working on this study will not belong to you.
- There is no plan for you to receive any financial benefit from the creation, use or sale of such a product or idea.

Agreement to be in this study and use my data:

I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study as described in this form. I understand and authorize the access, use and disclosure of my information as stated in this form. I know that being in this study is voluntary. I choose to be in this study: I will get a signed and dated copy of this consent form.

Subject Signature: _____ Date: _____

Subject Print Name:_____

I have explained the purpose of this study, the study procedures, the possible risks, discomforts and benefits. I have answered all questions regarding the study to the best of my ability.

Consent form explained by: _____ Date: _____

Print Name: _____

---------- Use Only if Applicable ----------

Signature Line for witness; required for consent of non-reading subjects and consent using a short form, if you requested such consent procedures

My signature below documents that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

Check applicable boxes:

Witness of Signature
Witness of consent process
An Interpretation took place

Interpreter/Witness Signature:_____ Date:_____

Interpreter/Witness Print Name: _____