INSTITUTE: National Cancer Institute

STUDY NUMBER: 11-C-0136 PRINCIPAL INVESTIGATOR: Christopher Kanakry, M.D.

STUDY TITLE: Multi-institutional Prospective Pilot Study of Lupron to Enhance Lymphocyte Immune Reconstitution Following Allogeneic Bone Marrow Transplantation in Post Pubertal Adults with Molecular Imaging Evaluation

Continuing Review Approved by the IRB on 06/05/20
Amendment Approved by the IRB on 06/04/20 (U) Date Posted to Web: 06/11/20

Donor

INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary.

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

If you are signing for a minor child, "you" refers to "your child" throughout the consent document.

Description of Research Study

<u>Your Evaluation for Donation of Cells</u>

On your first visit to the NIH Clinical Center, you will see a physician and other members of the transplant team. The doctor will take your medical history, perform a physical exam, and

explain the procedure. Approximately 4 to 10 teaspoons of your blood will be drawn to see if you and your relative are a good match. You and your relative must be a match on six of six genetic (hereditary) tests.

To donate cells, you must be in good health. If you have symptoms of heart disease, you cannot be a donor. If you have had any heart operations such as a bypass graft or angioplasty, a cardiologist must evaluate you and state that you are not putting yourself at risk by donating cells. If you have had cancer you may not be eligible to donate your stem cells. You must not have any infection in order to be a donor.

We will also test your kidneys and liver. As mentioned above, your blood will also be tested for Hepatitis B and C, syphilis, and a virus called cytomegalovirus (CMV). As part of this study, we will test you for infection with the human immunodeficiency virus (HIV), the virus that causes AIDS. If you are infected with HIV you will not be able to participate in this study. We will tell you what the results mean, how to find care, how to avoid infecting others, how we report HIV infection, and the importance of informing your partners at possible risk because of your HIV infection. Approximately 6-10 teaspoons of blood will be collected to perform these tests. The HIV, T. Cruzi (Chagas agent), and syphilis must be negative to be a donor. If you have a positive Hepatitis B or C test the study doctor will determine if you are allowed to be a donor. If you are a female able to have children, you will have a urine pregnancy test. Because of health risks to the fetus or newborns, pregnant or breastfeeding women cannot be donors.

We will also schedule an appointment to discuss the anesthesia for the marrow harvest.

How Stem Cells Are Collected: Your relative can receive the bone marrow of others to help them fight their cancer. That is why we are inviting you to donate cells from your bone marrow (called stem cells). If accepted by your relative's body, your stem cells will help their body begin to grow normal bone marrow cells.

The stem cells will be collected from the bone marrow in the operating room using anesthesia. Bone marrow will be obtained from the pelvis bones in the same way that a standard bone marrow test is performed. Needles will be inserted into the pelvis bones and liquid bone marrow will be drawn into syringes. The amount that will be collected will be based on the size of the transplant recipient and the white blood cell count performed on the bone marrow during collection. Approximately 1-2 teaspoons of marrow is required for every pound of recipient body weight. As much as 1500 mL (approximately 3 pints) may be needed. The anesthesia options (general anesthesia vs. spinal anesthesia), risks, and procedures will be discussed with you prior to the bone marrow collection and a separate consent will be obtained at that time. You may be admitted to the hospital the night before the bone marrow harvest depending on the scheduled time of the collection. You will remain in the hospital for 1 night after the harvest.

The Donation:

Once it is decided that you can be a donor, we will perform the procedure for immune cell collection under anesthesia.

Within one week after the bone marrow harvest or apheresis procedure(s), you will be checked for any side effects at the Outpatient NCI Clinic.

Research Performed on Donor Cells:

A small sample of the cell product that we collect will be tested for research purposes. We will remove approximately 5 million cells (less than 1% of the total) and study them to see what kinds of cells are in the donation product (for instance how many cells will become T cells or B cells). This will be compared with the cells that the recipient makes after the bone marrow transplant.

Birth Control:

Men and women who are sexually active on this study must agree to use an effective form of contraception (examples include: intrauterine device (IUD), hormonal (birth control pills, injections, or implants), tubal ligation/hysterectomy, partner's vasectomy, barrier methods (condom, diaphragm, or cervical cap), or abstinence while participating in this study.

Alternative Collection of Stem Cells

If it is not possible to perform the marrow harvest, donor stem cell collection may be performed by G-CSF stimulation. Such cases may involve donors who are medically not eligible to receive G-CSF or donors who prefer the marrow procedure relative to the apheresis procedure.

Risks or Discomforts of Participation

The main risk of bone marrow harvest relates to the need for anesthesia, which will involve either general anesthesia or spinal anesthesia. The specific risks of these procedures will be discussed in a separate consent procedure performed by the anesthesiology department. Bone marrow donation is very safe. The procedure commonly causes temporary pain and bruising over the sites where the marrow was collected. This usually can be managed with acetaminophen (e.g., Tylenol) alone. Occasionally, stronger pain medicines like codeine are required. Rarely, infection or bleeding at the needle sites may occur. Anemia due to removal of large amounts of bone marrow may require treatment with iron or a blood transfusion. Serious side effects of bone marrow harvest are extremely rare and include fat embolism (like blood clots in the lungs) and risks of anesthesia.

For patients who donate cells via apheresis or collection through the vein, there are different risks as detailed below.

G-CSF can cause the following side effects (these side effects stop once G-CSF has been stopped):

Likely:	Less Likely:	Rare:
• bone pain, • muscle aches, • headache	• Some people who receive G-CSF shots and apheresis have a low number of blood platelets for a short period of time. Platelets help your blood to clot. However, low platelet count from G-CSF has not caused an increased amount of bleeding. To be safe, your platelet count will be checked during and after the apheresis procedure. • Other common lab abnormalities have been seen but are reversible once G-CSF is stopped.	• allergic reactions, • chest pain, • lowering of the blood pressure • There is a very rare side effect (1 in 486,000 people) of one's spleen rupturing due to G-CSF.

Side effects of blood being drawn include pain and bruising in the area where the needle was placed, lightheadedness, or rarely, fainting. When too much blood is taken, one's red blood cell count may drop causing anemia. However, the amount of blood that you will donate in this study (a total of 20 teaspoons) should not cause anemia. To be safe, we will check your red blood cell level. If we find that you have anemia, we will give you treatment for this condition (in the form of iron tablets).

Side effects of the apheresis procedure may include low blood pressure. If this happens, we will adjust the apheresis machine to correct this problem. Other side effects include tingling in the mouth, fingers and toes, and mild muscle cramps. These discomforts can be stopped by adjusting or stopping the procedure. A rare, but potentially severe reaction may occur when calcium in the blood is low. Symptoms include: muscle spasm, facial twitching, abdominal pain, and severe feeling of "pins and needles". If this occurs, you will be treated immediately with IV calcium and the apheresis procedure will stop temporarily.

Side effects of a temporary I.V. in the femoral vein of the groin (if required) include bleeding, bruising, blood clot, or pain where the I.V. was placed. The I.V. will be placed only by physicians with experience in this procedure. They will discuss the risks with you before the procedure.

Potential Benefits of Participation

By being a donor, you will provide a source of stem cells and immune cells for your relative. Hopefully, your donation of cells will help his or her cancer treatment. Your participation may also help advance our understanding of stem cell transplants and improve the way that we treat cancer.

Alternative Approaches or Treatments

Collection through your veins after receiving a medication is an alternative approach to collection. For this, we will give you an injection (shot) of a drug called filgrastim or G-CSF for short. G-CSF is a protein normally produced by your body in small amounts. The U.S. Food and Drug Administration and the National Marrow Donor Program have both approved G-CSF for use in stem cell collection. It causes your stem cells to travel from your bone marrow into your blood. You will receive them in the arm or thigh. We will teach you or a family member how to give you these shots at home. They will be given for a period of 5, 6, or 7 days. Usually, you will be ready for the apheresis procedure for stem cell collection on day 5. Once the stem cells are in your blood, they can be taken from your veins using a process called apheresis. An I.V. (intravenous catheter) is placed into a vein in each of your arms. This will mean two needlesticks. Your blood will circulate through a machine that will collect and save your white blood cells and stem cells. The rest of your blood will go back into your body. The I.V. will be removed after the cells are collected. The whole procedure usually takes 4 to 6 hours. Apheresis avoids the need for an operation that would take the stem cells from your pelvis bone. It will be performed by trained personnel from the NIH Department of Transfusion Medicine.

Stopping Participation

The study doctor may decide to stop your participation in this study for the following reasons:

- If your doctor believes that it is in your best interest
- If you have request to be withdrawn
- If new information shows that another treatment would be better for your relative.

If this occurs, you will be informed of the reason therapy is being stopped.

What are the costs of taking part in this study?

If you choose to take part in the study, the following will apply, in keeping with the NIH policy:

- You will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done outside the Clinical Center, NIH if the study related treatment is not available at the NIH.
- There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. You may have to pay for these costs even if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the Clinical Center, NIH.

Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

Research Subject's Rights

It is your choice to participate in this research study. You may quit the study at any time. There are no penalties for quitting the study. We encourage you to ask our staff any questions that you might have.

Certificate of Confidentiality

To help us protect your privacy, we have obtained a Certificate of Confidentiality. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

You should also know that there are several circumstances in which the Certificate does not provide coverage. These include when information:

- will be used for auditing or program evaluation internally by the NIH; or
- must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA).
- is necessary for your medical treatment and you have consented to this disclosure;
- is for other research.

In addition, identifiable, sensitive information protected by this Certificate cannot be admissible as evidence or used for any purpose in any action, suit, or proceeding without your consent.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.

Use of Specimens and Data for Future Research

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is

stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that it may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

OTHER PERTINENT INFORMATION

1. Confidentiality. When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

2. Policy Regarding Research-Related Injuries. The Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

3. Payments. The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

4. Problems or Questions. If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Christopher Kanakry, M.D., Telephone: 240-760-6171. You may also call the Clinical Center Patient Representative at (301) 496-2626. If you have any questions about the use of your specimens or data for future research studies, you may also contact the Office of the Clinical Director, Telephone: 240-760-6070.

5. Consent Document. Please keep a copy of this document in case you want to read it again.

COMPLETE APPROPRIATE ITEM(S) BELOW:

A. Adult Patient's Consent

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

Signature of Adult Patient/ Legal Representative _____ Date _____

Print Name _____

B. Parent's Permission for Minor Patient.

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study.
(Attach NIH 2514-2, Minor's Assent, if applicable.)

Signature of Parent(s)/ Guardian _____ Date _____

Print Name _____

C. Child's Verbal Assent (If Applicable)

The information in the above consent was described to my child and my child agrees to participate in the study.

Signature of Parent(s)/Guardian _____ Date _____ Print Name _____

THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM JUNE 05, 2020 THROUGH JUNE 04, 2021.

Signature of Investigator _____ Date _____

Print Name _____

Signature of Witness _____ Date _____

Print Name _____