

INSTITUTE: National Cancer Institute

STUDY NUMBER: 11-C-0073 PRINCIPAL INVESTIGATOR: Nirali N. Shah, M.D.

STUDY TITLE: A Phase I Study of NK Cell Infusion Following Allogeneic Peripheral Blood Stem Cell Transplantation from Related or Matched Unrelated Donors in Pediatric Patients with Hematologic Malignancies

Continuing Review Approved by the IRB on 08/21/17

Amendment Approved by the IRB on 01/08/16 (P)

Date Posted to Web: 09/26/17

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.

Why is this study being done?

In the body, there are "stem cells" which mature into the cells of the blood. These stem cells, which are found both in the bone marrow and in the blood stream, can be collected and transplanted to treat a variety of types of cancer. This is called hematopoietic stem cell

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transplantation (HSCT). The transplanted stem cells travel to the patient's bone marrow and begin producing normal blood cells. In addition, transplanted immune cells from the donor can attack the patient's cancer cells. We are asking you to donate stem cells to be used in an experimental type of HSCT for an individual with cancer which has not responded to previous treatment. After you donate your cells we will separate them into two portions. One will be prepared for the HSCT and the other portion will be prepared from your white blood cells (donor lymphocytes) to make 'Natural Killer' Cells or NK-DLI (Donor Lymphocyte Infusion). In the laboratory NK cells have been shown to kill tumor cells, but we do not know if this will occur when given to patients after HSCT. The NK-DLI portion of this study is experimental and has not been approved by the US Food and Drug Administration (FDA) for the treatment of cancer, but the FDA has given us permission to use these types of cells in this research study.

Why are you being asked to take part in this study?

We are asking you to donate stem cells to be used in an experimental type of HSCT for an individual with cancer which has not responded to previous treatment.

How many people will take part in this study?

A maximum of 43 recipients and 43 donors will be enrolled onto this study.

Description of Research Study**What will happen if you take part in this research study?****Evaluation for Donation**

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 a medical history, perform a physical exam, and explain the procedures. Blood and urine testing will also be performed. Donors and recipients must be closely matched as determined by special blood immune typing, called "HLA typing." In order to donate, you must match the recipient HLA types, but identical twins may not be donors in this study because it may confuse the results. To serve as a donor, you must also be in good health. There are a number of conditions that would prevent someone from being a donor, for example heart disease or certain kinds of infection. You will be tested for a number of infections that can be spread through the blood including Hepatitis B and C, cytomegalovirus (CMV), syphilis, and HIV (the virus that causes AIDS). 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 newly diagnosed HIV infection, and the importance of informing your partners at possible risk because of your HIV infection.

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Potential donors under the age of 18 will meet with a social worker and mental health specialist (psychologist or psychiatrist) to discuss possible donation. The results of your donor evaluation will be discussed with you. If any of the findings prevent you from being a donor, this will be explained. If any of the results suggest that you should undergo further evaluation or treatment, we can refer you for appropriate medical attention. If you are a woman of childbearing age, you will need to take a urine pregnancy test. Because of health risks to the fetus or newborns, pregnant or breastfeeding women cannot be donors. While receiving filgrastim and until stem cells are collected it is important to use adequate contraception (either a barrier method or a prescribed hormonal method (birth control pills, injectable methods, etc.)).

How Stem Cells Are Collected

In order to donate stem cells, you will need to receive injections (shots) of a drug called filgrastim or G-CSF. Filgrastim is a natural substance produced artificially in the laboratory using DNA technology (i.e., the gene for G-CSF has been inserted into E. Coli bacteria which produces the drug in large quantities). The U.S. Food and Drug Administration and the National Marrow Donor Program have both approved filgrastim for use in stem cell collection. Filgrastim causes your stem cells to travel from the bone marrow into the blood. Filgrastim will be given by subcutaneous injection (a shot under the skin much like insulin) once a day. We will teach you or a family member how to give these shots at home, or if needed, a nurse can administer the filgrastim. The shots will be given in the arm or thigh. They will be given for a period of 5, 6, or 7 days. Usually, you will be ready for the stem cell collection on day 5. A blood test will be drawn on the morning of the planned donation to help us decide when to start collection.

The stem cells will be collected from the veins on a machine that can separate blood. This is known as "apheresis." The procedure is similar to that routinely used for donation of platelets, another type of blood cell. In order to collect the stem cells, an I.V. catheter (needle or plastic tube temporarily placed in a vein) will be put into each of your arms. This requires two needle sticks. Sometimes the arm veins cannot be used for collection, in which case it would be necessary to insert a special I.V. known as a central venous catheter (CVC) into a large vein in the neck or groin area. If that is required, a separate consent will be obtained. In attempt to avoid this, the veins in the bends of your arms should not be used for blood drawing until after donation is completed if possible.

Your blood will circulate through a machine that will collect some of the white blood cells and stem cells. The rest of your blood will be returned back into your body along with a small amount of salt solution (saline) and blood thinning medication (anticoagulant). Blood thinning medications, heparin and/or citrate anticoagulant, will be used to keep your blood from clotting during the procedure. Each apheresis procedure usually takes 4 to 6 hours to complete. Enough stem cells to perform the HSCT can usually be collected during a single apheresis. Sometimes, it is necessary to continue the filgrastim shots and repeat the apheresis on the next day (day 6). Rarely, a third apheresis on day 7 may be required. In the unusual case that we still do not have enough cells to perform the transplant, we will ask that you rest for two weeks before repeating

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the filgrastim shots and apheresis. Apheresis will be performed by trained personnel from the NIH Department of Transfusion Medicine (DTM). The I.V. tube(s) will be removed after the cells are collected. If both a CVC and more than one day of collection are required, you will need to remain in the hospital for 1-2 nights as necessary until the collections can be completed and the catheter can be removed.

Within one week after the apheresis procedure(s), you will have a check up at the NIH Outpatient Clinic or your regular physician.

Your collected cells will typically be given to the recipient by the next day for the transplant. In addition, a very small portion of the cells collected will be saved for potential future use and another small portion will be used to perform scientific studies related to cancer and will not be transplanted, and as previously mentioned, your cells will be divided in two portions. One portion will be used for the HSCT and one portion will have special cells selected, called 'Natural Killer' (NK) cells which will be grown to larger numbers in the laboratory and given back to the patient in two (2) infusions.

Occasionally it is necessary to go back to the donor to request additional cells that are needed to treat the recipient. If such a situation should arise, the reason for the additional cells will be discussed with you and your physician will determine the therapy required and the best method of collection.

Alternative Approaches or Treatments

What other choices do I have if I do not take part in this study?

Stem cells can also be collected from the bone marrow in the hipbones. This would be performed in the operating room using anesthesia. Most donors prefer apheresis over a bone marrow donation. You can refuse to donate stem cells. If you refuse, a HSCT might not be able to be performed unless another suitable donor could be found.

Risks or Discomforts of Participation

What side effects or risks can I expect from being in this study?

Stem cell donation is a safe procedure that is routinely performed in healthy children and adults. There are a number of potential discomforts and side effects that are associated with donation.

Filgrastim has been used in humans since the late 1980's and it has been shown to be very safe. However, this medication has the potential to cause side effects. Almost always, the side effects are minor and go away on their own when filgrastim is stopped. The common side effects include pain or bruising at the injection sites, bone pain, and muscle aches. Less likely side effects include fever, chills, headaches, tiredness, enlargement of the spleen, and elevations in certain blood tests (uric acid, LDH, alkaline phosphatase). Temporary worsening of pre-existing

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inflammatory conditions such as psoriasis has occurred in some individuals who received filgrastim. Rarely, filgrastim can cause allergic reactions and a lowering of the blood pressure.

The most common side effects of apheresis are pain and bruising at the IV needle sites. Side effects of a temporary I.V. in the vein of the groin (if required) include bleeding, bruising, infection, blood clot, or pain. Medical personnel with experience in this procedure will place the I.V. They will discuss the procedure and possible risks in further detail with you before the procedure. Mild side effects from the blood thinning medication citrate are common and include chills, numbness and tingling sensations ("pins and needles") especially around the mouth, anxiety, muscle cramps, and nausea. These rapidly go away when the collection is slowed down. More serious side effects due to citrate-induced low calcium levels are uncommon and include low blood pressure, seizures, weakness, and muscle stiffness. If this happens, the apheresis procedure will be stopped, in which case these side effects quickly go away. You will be monitored closely for any side effects and the procedure will be stopped and appropriate treatment administered if necessary.

Some people have a low number of blood platelets for a short period of time after donation. Platelets help the blood to clot. However, low platelet counts from stem cell donation have not caused an increased amount of bleeding. To be safe, your platelet count will be checked during and after the apheresis procedure.

Side effects of blood draws include pain and bruising in the area where the needle was placed, lightheadedness, and rarely, fainting. When a large amount of blood is drawn, the red blood cell count may drop causing anemia. However, the amount of blood that you will donate in this study (a total of approximately 20 teaspoons) should not cause anemia. To be safe, we will check your red blood cell count before and after collection. If we find that you have anemia, we will prescribe iron tablets.

Potential Benefits of Participation

Are there benefits to taking part in this study?

There are no direct benefits to the donor. It is hoped that your donation of cells will lead to an improvement in the patient's cancer. Your participation may also help advance our understanding of stem cell transplants and improve the way that we treat cancer.

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.

The National Institutes of Health reviews NIH staff researchers at least yearly for conflicts of interest. The following link contains details on this process

PATIENT IDENTIFICATION**CONTINUATION SHEET for either:**

NIH-2514-1 (07-09)

NIH-2514-2 (10-84)

P.A.: 09-25-0099

File in Section 4: Protocol Consent

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<http://ethics.od.nih.gov/procedures/COI-Protocol-Review-Guide.pdf>. You may ask your research team for additional information or a copy of the Protocol Review Guide.

You will have your blood drawn during the stem cell donation and we would like to keep some of the blood and your data that is left over after preparation for the transplant for future research. Your blood specimens and data will be identified by a number and not your name. The use of your specimens and data will be 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 decide now that your specimens and data can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your specimens and data. Then any blood specimens that remain will be destroyed and your data will no longer be used.

Please read each sentence below and think about your choice. After reading each sentence, circle and initial the answer that is right for you. No matter what you decide to do, it will not affect your care.

1. My blood specimens and data may be kept for use in research to learn about, prevent, or treat cancer.

Yes No Initials _____

2. My blood specimens and data may be kept for use in research to learn about, prevent, or treat other health problems (for example: diabetes, Alzheimer's disease, or heart disease).

Yes No Initials _____

3. Someone may contact me in the future to ask permission to use my specimen(s) and/or in new research not included in this consent.

Yes No Initials _____

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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, Nirali Shah, M.D., Building 10-CRC, Room 1-1621, Telephone: 301-451-0390. 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: 301-496-4251.

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 AUGUST 21, 2017 THROUGH AUGUST 20, 2018.**

Signature of Investigator

Date

Signature of Witness

Date

Print Name

Print Name