Official Title: Haploidentical Stem Cell Transplant Using Post Transplant Cyclophosphamide for GvHD Prophylaxis: A Pilot Study
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HAPLOIDENTICAL STEM CELL TRANSPLANT USING POST TRANSPLANT CYCLOPHOSPHAMIDE FOR GVHD PROPHYLAXIS: A PILOT STUDY

Informed Consent Form to Participate in Research
Dianna S. Howard, MD, Principal Investigator

INTRODUCTION

You are being invited to participate in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You may or may not receive any benefit from being a part of this study. There may also be risks associated with being part of research studies.

You are being asked to take part in this study because you are a candidate for a procedure called Hematopoietic Stem Cell Transplantation (HSCT) and someone in your family has agreed to be your donor. Your participation is voluntary. Please take your time to make your decision; your study doctor or the study staff will explain any information that you do not understand.

WHY IS THIS STUDY BEING DONE?

Hematopoietic Stem Cell Transplant (HSCT) means that you will be infused (transplanted) with stem cells from another person, or donor. HSCT is a standard treatment option and offers a good chance of cure for blood diseases (leukemias.) However, a side effect of the transplant is Graft vs. Host Disease (GvHD), a life-threatening condition where the infused stem cells attack you because they do not 'recognize' your body's own cells. The risk of GvHD gets higher the more your donor's HLA markers do not match yours. HLA, or Human Leukocyte Antigens, are molecules that make up your immune system and are found on your white blood cells. Unfortunately, less than 1/3 of all patients who need a stem cell transplant have a fully HLA-matched donor. For this reason, a transplant with a half HLA-matched donor is usually preferred, and is called a "haplo-identical" transplant. Since your biological mother, father, sisters, or brothers share at least half of your genetic information, the best "haplo" donors are your family members – this is called "familial haplo-identical" transplant or, more commonly, a "half-matched related" transplant.

This pilot study will explore the effects (good or bad) of familial haplo-identical transplants at Wake Forest Baptist Health and see how well it will treat your cancer and improve your condition. You are eligible for this study because your doctor has determined that a half-matched related transplant is the best treatment option for you.

To avoid the risks associated with half-matched related transplants, you will be given a drug called cyclophosphamide on days 3 and 4 after your transplant. Cyclophosphamide is FDA approved to treat many different types of cancers, including hematologic malignancies. Treatment with cyclophosphamide immediately after a half-matched related transplant is

regarded as the best way to reduce the risk of GvHD and treat your cancer. Therefore, another goal of this study is to see if giving you cyclophosphamide after your half-matched related transplant is safe and effective in treating your cancer and decreasing your chances of getting GvHD.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

Approximately 24 people will take part in this study.

WHAT IS INVOLVED IN THE STUDY?

If you take part in this study, you will provide informed consent and have a medical history review. As part of the research study, you will have your half-matched related stem cell transplant at Day 0. Then, on days 3 and 4 after your transplant, you will receive cyclophosphamide. You will be followed up to 2 years from your stem cell transplant to monitor your outcome and health.

HOW LONG WILL I BE IN THE STUDY?

You will have follow-up visits as part of the normal standard of care for up to 2 years after your transplant. Therefore you will be in the study for approximately 2 years plus the time it takes to set up and receive your half-matched related transplant after signing this consent.

WHAT ARE THE RISKS OF THE STUDY?

Potential Risks of Stem Cell Transplants

The treatment with blood or bone marrow transplant requires the use of powerful drugs (chemotherapy) that have side effects, some potentially very serious. It will be necessary for you to be admitted to the hospital for approximately 6-8 weeks.

In as many as 20-30% of patients undergoing blood or bone marrow transplantation, a combination of Graft versus Host Disease (GvHD), treatment thereof, other infections, and side effects of chemotherapy may lead to death in the first few months following transplantation. Drugs such as cyclosporin, methotrexate, and prednisone are given to try to prevent GvHD and many therapies are available to treat GvHD if it should develop. Specific details of prevention and treatment of GvHD will be discussed separately from this consent form.

Potential Risks of Using Cyclophosphamide

Bone Marrow Suppression: The treatment used to kill cancer cells and the GvHD-causing cells after transplant may also kill some normal body cells, especially those that grow rapidly (blood cells, hair, cells that line the mouth, stomach and intestines). Blood cells are made in the bone marrow and are responsible for fighting infections (white blood cells), carrying oxygen (red blood cells), and causing blood to clot (platelets). A reduction in the number of these blood cells (marrow suppression) can lead to an increased risk of bleeding and infection. When these effects occur, they can be treated with blood products (transfusions) and antibiotics. Bone marrow suppression is an expected side effect after receiving high doses of cancer-killing drugs, and it is this serious drug reaction that requires bone marrow transplantation.

The transplanted blood or marrow cells will replace the cells damaged by chemotherapy usually in 3-5 weeks; however, if the transplant is not successful, recovery of your marrow function may not occur and death due to an infection or bleeding is more likely.

In addition, these medications suppress the immune system to allow you to accept the blood or marrow cells from your donor. This suppression of the immune system will, however, also make you more susceptible to infections after the blood or marrow transplant. Even if the bone marrow appears to be functioning well, your immune system does not respond normally until at least one year after transplantation.

Heart Failure: A small number of patients given cyclophosphamide in high doses have developed shortness of breath and swollen ankles because of heart weakness. On rare occasions, death due to heart failure can occur.

Lung Damage: Scarring of the lungs (fibrosis) or inflammation (pneumonitis) may occur resulting in cough or shortness of breath and rarely can lead to death due to lung failure.

Liver Irritation: High doses of chemotherapy may be associated with inflammation of the liver. This is usually temporary, but rarely severe liver damage is produced which can be fatal.

Kidney Damage: Kidney damage is minimized by giving fluids by vein. Kidney function will be monitored with blood tests. Kidney damage is usually reversible, but may not be or take a long time to resolve.

Bladder Irritation: Cyclophosphamide may produce burning on urination or bloody urine. You should receive by vein at least three liters of fluid (approximately 12 glasses) daily. Empty your bladder frequently. Bladder irritation is usually reversible, but rarely severe damage occurs which can be fatal. Patients with severe damage may need to have their bladders removed.

Skin Changes: Many patients who receive high doses of chemotherapy develop a rash. Later, the skin may peel. A variety of creams may lessen the symptoms. Sometimes the skin changes resemble mild sunburn followed by darkening which may be permanent.

Hair Loss: Hair will fall out 1-3 weeks after the first dose of chemotherapy but will usually grow back several months after chemotherapy is discontinued. Hair color will not dramatically change, but sometimes the hair is darker and curlier.

Irregular Menstrual Cycle: The menstrual cycle may usually cease permanently resulting in an inability to become pregnant. Birth control should be practiced for at least 1 year following this therapy, if fertility is maintained.

You should tell the research staff about all the medication, vitamins and supplements you take and any medical condition you have. This may help avoid side effect, interactions and other risks. You should talk to your study doctor about any side effects that you have while taking part in the study.

Reproductive Risks:
The drugs used in this study are known to have risk of causing malformations in an unborn child, especially when given in the early part of pregnancy. Therefore, you should not become pregnant or father a baby while on this study. For this reason, both men and women will be asked to practice an effective method of birth control while you are participating in this study. Also, because the risk is unknown to young children, you should not nurse your baby while on this study. Ask about counseling and more information about preventing pregnancy.

Due to unknown risks and potential harm to the unborn fetus, sexually active women of childbearing potential must use a reliable method of birth control while participating in this study. Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, intrauterine device (IUD), DepoProvera, Norplant, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and spermicidal foam or gel and/or a cervical cap or sponge. We encourage you to discuss this issue further with your physicians if you have any questions.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct benefit to you. We hope the information learned from this study will benefit other people in the future. The benefits of participating in this study may be: cure of your cancer and prevention of Graft vs Host Disease.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to receive treatment. You should talk to your doctor about all the choices you have. Instead of being in this study, you have these options:

- Other chemotherapies
- Comfort care, which is an option if you decide that you do not want any more active treatment for your cancer. Comfort care includes pain medication and other types of support. It aims to maintain your comfort and dignity rather than cure disease. Usually this care can be provided at home. If you think you might prefer comfort care, please discuss this with your family, friends, and your doctor.

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes: medical history, medical images, how you respond to study procedures, laboratory and other test results, and physical examinations. If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study will be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer. Only the following people or organizations will be granted access to your Protected Health Information:

1. The study investigator and his/her staff, or others at Wake Forest University Health Sciences who oversee research.

2. Other people or laboratories providing services for this research project on behalf of Wake Forest University Health Sciences and Wake Forest University Baptist Medical Center.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state law.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for an indeterminate period of time. This authorization does not expire. Any research information entered into your medical record will be kept for as long as your medical record is kept by the Medical Center. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.
You can tell Dr. Howard that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Dianna S. Howard, MD
[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.
By signing this form you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this

information limited to individuals with proper authority, but who may not be directly involved with this research study.

WHAT ARE THE COSTS?

There are no costs to you for taking part in the research portion of this study. However, the costs for the half-matched related transplant and cyclophosphamide as well as the follow-up office visits are considered 'regular medical care' procedures and will be billed to you or your insurance.

WILL YOU BE PAID FOR PARTICIPATING?

You will receive no payment or other compensation for taking part in this study.
Parking validation will be provided for all study-related visits.

WHO IS SPONSORING THIS STUDY?

Wake Forest University Health Sciences is sponsoring the conduct of this study. The researchers do not, however, hold a direct financial interest in the sponsor or the product and procedures being studied.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call Dr. Howard at [redacted]

WHAT ARE MY RIGHTS AS A RESEARCH PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because it is not in your best medical interest, your condition worsened, new information becomes available, you had an unexpected reaction, or because the entire study has been stopped.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Dr. Dianna Howard, at [redacted].

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted].
You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Obtainer Signature:_____ Date:_____ Time:_____ am pm