PRINCIPAL INVESTIGATOR: Steven Pavletic, MD

STUDY TITLE: A Phase I/II Open Label, Dose Escalation Study of Palifermin (Kepivance) In Persons Undergoing Unrelated Donor Allogeneic Hematopoietic Cell Transplantation

STUDY SITE: NIH Clinical Center

Cohort: *Treatment*

Consent Version: *4/7/2022*

WHO DO YOU CONTACT ABOUT THIS STUDY?

Principal Investigator: Steven Pavletic, MD
240-760-6174
pavletis@mail.nih.gov

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. 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). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

If the individual being asked to participate in this research study is not able to give consent to be in this study, you are being asked to give permission for this person as their decision-maker. The term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research, throughout the remainder of this document.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

We are conducting a study of allogeneic stem cell transplantation from HLA-matched unrelated, volunteer donors for cancers of the blood and immune system.

"Stem cells" are immature blood cells, like seeds; they grow in the bone marrow and produce all of the cells needed for normal blood and immunity. When these stem cells are taken from one

person (called the "donor") and given to another person (called the "recipient"), it is known as "allogeneic" stem cell transplantation (SCT). Originally, stem cells were collected for transplantation by taking samples of bone marrow from the donor. This was commonly called "bone marrow transplantation." Now, most allogeneic transplants use stem cells collected from the donor's circulating blood.

Allogeneic stem cell transplantation (SCT) has been used successfully to treat, and sometimes cure, many kinds of cancer or pre-cancerous conditions that develop in blood or immune system cells. Large doses of chemotherapy drugs and/or radiation have been traditionally used to eliminate most of the cancerous or abnormal cells from the recipient's system, along with most of his or her own stem cells and immune cells. Donor stem cells can then replace the recipient's stem cells in the bone marrow, restoring normal blood production and immunity; this process is called "engraftment". In this way, an allogeneic SCT provides not only new blood cells but an entire new immune system. Immune cells from the donor are important not only to protect the transplant recipient from infections; these transplanted cells can sometimes eliminate the abnormal cells that caused the patient's disease. This type of immune attack is called the "graft- versus-tumor" (GVT) effect, and it is thought to be the main reason that allogeneic SCT cures some patients of these conditions.

If the recipient's immune system remains strong enough after large doses of chemotherapy or radiation, it may attack and destroy the donor's cells after the transplant. This is called "graft rejection." When this happens, the transplant recipient's own stem cells may be so severely damaged after chemotherapy or radiation that they cannot produce blood cells, usually leading to death. Another serious complication can occur if donor immune cells recognize and attack the recipient's normal tissues, damaging the liver, intestinal tract, and skin. This type of immune attack is called "graft-versus-host disease" or GVHD.

Graft rejection or GVHD after allogeneic SCT are less likely when the transplant recipient and donor are very similar genetically. To measure how genetically similar a recipient and donor are, both persons are tested to identify protein markers on the surface of their blood cells and other body tissues. These markers are called "human leukocyte antigens", or HLA. A person inherits half of his or her HLA markers from each parent. Your immune system uses HLA proteins on your body's cells to tell the difference between normal, healthy tissues and foreign organisms like bacteria or viruses. Differences in HLA proteins between a donor and recipient make it more likely that one person's immune system will recognize the other person's cells as foreign, causing graft rejection or GVHD. A donor and recipient who share all 8 of their HLA markers are called "HLA-identical". A transplant from an HLA-identical sibling (brother or sister) has a lower chance of graft rejection or GVHD, compared with other unrelated donors for allogeneic SCT. Many people have cancers that could be treated with allogeneic SCT, but only 20-30% of people have HLA-identical sibling donors. For some people without HLA-identical sibling donors, an HLA-matched unrelated donor can be used, but the risk of graft rejection and GVHD is higher.

Severe GVHD is the leading cause of death in patients who receive an allogeneic SCT. Drugs can prevent GVHD after allogeneic SCT, but they do not work all the time.

We are trying to improve the results of allogeneic SCT from HLA-matched unrelated donors.

The main purpose of this study is to study if high doses of palifermin given just prior to chemotherapy conditioning in increasing doses could be administered safely, prevent chronic GVHD and improve immunological function after transplant. Palifermin is a drug approved by the FDA for the prevention of mouth pain and swelling after transplantation, but is investigational in this particular study.

In the first part of the study, the phase 1 portion, we will give palifermin at increasingly higher doses in order to find the highest dose that is still safe for patients. The first three subjects enrolled (or six if one of the first three has an intolerable side effect) will be given the starting dose of palifermin. If 0 of 3 or 1 of 6 subjects has an intolerable side effect, then three (or six) more subjects will be enrolled at the next highest dose level. If two or more subjects has an intolerable side effect, no other subjects can be enrolled at the dose level. Doses will continue increasing until there are two intolerable side effects at a dose level or we have reached the highest dose planned in the study.

Once we have determined the highest safe dose, we will proceed to the phase 2 portion of the study. In this part of the study, additional subjects will be enrolled at the highest safe dose to test whether the higher dose is more effective in preventing chronic GVHD and improving immunological function after transplant.

If we are required to stop this study because too many patients have serious side effects, we will continue to provide care for you according to the study protocol.

WHY ARE YOU BEING ASKED TO TAKE PART IN THIS STUDY?

This research study is for patients with a blood or bone marrow cancer that meet transplant requirements, but who do not have an HLA-matched sibling and who have had a potential HLA-matched (at 8/8 markers) unrelated donor identified through one of the bone marrow donor registries such as the National Marrow Donor Program.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 50 patients will take part in this research study.

DESCRIPTION OF RESEARCH STUDY

Before you begin the study

We will perform some tests to determine whether you are eligible for the study. These tests will be explained on a separate consent. Most of the tests would have been done as part of your standard medical care; however, specific to this protocol, about 5 to 10 tablespoons of blood will be drawn to check how closely you and your donor are genetically matched. Often this blood test has already been performed at your home medical office prior to a visit to the NIH or it will be performed at the NIH Clinical Center.

During the study

Once it is determined that you are eligible for the study, you will undergo the following tests/exams to help us manage your health and monitor your condition while you are on the study. These tests will be done before you undergo your induction therapy.

- Test for viruses and other infectious organisms

- Routine blood tests and urine tests
- Pregnancy test (if you are a woman who can have children)
- Evaluation for central vein access (described below)
- Blood test to assess immune system
- Nutritional assessment
- Dental exam
- Eye exam
- Social work assessment
- GYN exam (for female subjects)
- Gastroenterology consult

The Central Venous Catheter

If you do not already have one before you enroll in this study, you will receive an intravenous (I.V.) line placed. This line is called a central venous catheter that can be used throughout your transplant procedure and follow-up treatment. If the catheter becomes infected or clogged, it can be replaced. It will be flushed once daily to prevent clogging and the dressing changed weekly. The nursing staff will teach you or your caregiver how to do this yourself.

The catheter will be used to give you chemotherapy, your transplant, donor lymphocyte infusion (DLI) (if needed), blood transfusions (if needed), and other medications such as antibiotics. It can also be used for drawing blood samples for tests. Since blood will be drawn often during your treatment, the catheter will make it easier and less painful.

Lumbar Puncture (optional)

You may undergo a lumbar puncture (also called a spinal tap) to remove a small amount of spinal fluid (about 1-2 teaspoons) that will be used for diagnostic testing. A lumbar puncture can help diagnose serious infections and other disorders. A lumbar puncture is done by inserting a small sterile needle through the skin and muscle, going between the bones of the spine in the lower back until the needle punctures the spinal canal covering. The spinal fluid will then drain out through the needle on its own.

Induction Chemotherapy

In this study you will receive one to three cycles of induction chemotherapy (based on the type of disease you have) to treat your disease and to weaken your immune system. If the study doctors feel your immune system is already weakened and your disease is well controlled you may not receive induction chemotherapy.

For patients with chronic lymphocytic leukemia, pro-lymphocytic leukemia, multiple myeloma, and most forms of lymphoma, this chemotherapy will include the following drugs: fludarabine, cyclophosphamide, etoposide, doxorubicin, vincristine, and prednisone (also called: "EPOCH-F"). Patients with lymphoblastic lymphoma, acute myelogenous leukemia, acute lymphocytic leukemia, chronic myelogenous leukemia, and other "pre-leukemic" diseases will receive induction chemotherapy with fludarabine, cytarabine, and filgrastim (also called: "FLAG").

Patients with certain forms of lymphoma and leukemia may also receive a drug called rituximab. Each of these medications has been approved by the Food and Drug Administration (FDA). The

study doctors will test a biopsy specimen from your cancer to help them decide if you should receive rituximab with your induction chemotherapy. To start, you will receive common doses of these drugs for five days followed by a 16-day (EPOCH-F) or 23-day (FLAG) rest period (this time period is 1 cycle). The EPOCH-F regimen is generally given in outpatient setting. The FLAG regimen is given in the hospital, so you will be admitted as an inpatient, and you will remain in the hospital until your blood counts recover, usually 3 to 4 weeks. The effect of the chemotherapy on your immune system and on your disease will determine how many cycles of induction chemotherapy you receive. If blood tests show that your immune system is weakened enough after one cycle, you will go directly to the transplant. If your immune system is not very weakened and your disease is not growing after one cycle of induction chemotherapy, you will receive one or two more cycles (5 days of the same chemotherapy you received for cycle 1, followed by 16 (EPOCH-F) or 23 (FLAG) days of rest per cycle). If your disease grows in spite of the induction chemotherapy then the induction chemotherapy will be stopped, and you will be removed from the study. If your white blood cell count remains low for a long time after induction chemotherapy, meaning your immune system has weakened, you will go directly to the transplant. At most, you will receive 3 cycles of chemotherapy. In the unusual circumstances and/or if necessary, your doctors may decide to use some other standard drugs or combination prior your transplant to achieve best control of your cancer.

Transplant

Once you have completed your induction chemotherapy (if needed), you will undergo additional tests to determine whether you are eligible to proceed with the transplant. This portion of the study includes which includes palifermin, the conditioning regimen and the transplant.

These tests/evaluations include:

- Medical history/physical exam
- Confirmation of a matched unrelated donor
- Tests to determine whether your cancer has gotten better or worse or stayed the same
- CT scan of chest (for research)
- Routine blood tests

After it has been confirmed that you are eligible to proceed to the research phase, you will undergo the following.

<u>Pre-transplant</u>

You will receive one dose of palifermin intravenously 7 days before you are scheduled for transplant.

On the following day, you will begin 4 days of reduced-intensity transplant chemotherapy, also called the "conditioning regimen," to prepare you for the transplant. This consists of a regimen of FDA approved agents, fludarabine, cyclophosphamide, mesna and furosemide. These will be administered intravenously.

Beginning three days before you receive the stem cell transplant, you will receive the drugs tacrolimus and sirolimus to help prevent GVHD. Sirolimus is given by mouth once a day for approximately six months after transplant. Tacrolimus is given either through an I.V. or by mouth once a day for approximately six months after transplant. Methotrexate is given for four doses

intravenously (through the vein) before you are discharged from the hospital, shortly after the transplant.

2 days after completing conditioning chemotherapy, you will receive the transplant with your unrelated donor's stem cells.

Collection of the Blood Stem Cells from Your Donor

Before you begin your induction chemotherapy, your unrelated donor will have had a medical examination by a doctor in the National Marrow Donor Program (NMDP) network that includes extensive testing to make sure they do not have any of the following: HIV, Hepatitis B, Hepatitis C, and possible infectious diseases that may be transmitted by stem cell donation. The donor's exam will also ensure that they remain available and are physically well enough to undergo the donation procedure. The NMDP will notify NIH if there are any abnormalities that increase the risk of transmitting infectious diseases to you during the transplant. These findings will be discussed with you. The donor's medical clearance will be verified by the NIH study doctor before you begin the research phase of the study.

Unrelated donor transplants are confidential and the identity of the donor will be anonymous. This means that you will not know who your donor is or where they are. You will know the age and gender of the donor and any history or medical exam findings that could possibly change the risk of your transplant. Likewise, the donor will not know who you are or where you are. S/he will know your age, gender, and the type of disease that you have. The donor will be given basic updates about your condition 30 days, 6 months, and 1 year after your transplant. The only information they will receive is whether or not the stem cells "engrafted" (taken hold), and if you have been discharged from the hospital. The donor will also be notified in the event of your death.

Depending on the policy of the particular donor center, you may be able to communicate without revealing your identities in an anonymous manner with your donor beginning at the time of your transplant. In some cases, if both you and the donor agree, you may be able to learn who your donor is after one year. There are some cases when a donor and patient may never communicate or meet. Your transplant coordinator will tell you the details of if and how you may contact the donor once the donor has completed his or her medical exam.

Rarely, a volunteer donor may become unavailable or the donor apheresis center is unable to collect enough stem cells to perform the transplant. If this happens, you will be removed from the study but we will continue to care for you if you have already received conditioning therapy.

Transplant Procedures

While you are in the hospital for your transplant, you will be monitored very closely for possible complications, which are described below. You will receive drugs to help manage these complications. Blood will be drawn frequently during your treatment. Your blood will be tested to monitor your health during and after the chemotherapy and transplant procedure. In general, 4 to 10 teaspoons of blood will be drawn an average of 2 to 3 times per week. Some blood will be drawn for research purposes. In general, 3 to 4 tablespoons of blood will be drawn for research on average of once per week for the first 100 days after transplant.

After you have had your transplant

You will be hospitalized approximately 3-4 weeks after your transplant, but it could be longer if there are any complications. You will be required to remain in the Washington, D.C. area for approximately three months after transplantation so the NIH doctors can monitor you in case of any complications. You may require re-admission to the hospital for complications.

After the transplant, if tests show that your blood and immune cells have not fully converted to your donor's type ("mixed chimerism"), then the drugs you are taking to prevent GVHD will be lowered to help change your blood and immunity to full donor chimerism. Sometimes additional therapies such as DLI may be given to you intravenously (I.V.) to reach a state of full donor chimerism, as described above. If your cancer is still present or grows after the transplant, tacrolimus may be reduced in an attempt to permit a stronger graft-versus-tumor effect. After this, if there are no signs of significant GVHD, then you may receive one or more DLI at increasing doses. These DLI are intended to "boost" your new immune system and can enhance the graft-versus-tumor effect in some, but not all, patients. DLI can sometimes lead to the development of GVHD, so we will monitor you very closely for signs of GVHD after these infusions. If you experience significant GVHD after a DLI, we will give you treatment for GVHD, but you will not receive any further DLI. You may also be eligible to receive chemotherapy or other standard therapy (like radiation therapy or immune therapies) after the transplant if your cancer requires further treatment. This therapy can be given alone or combined with DLI.

You will continue on medications at home to lower the risk of GVHD and infections.

If you are in good health after the three month period after your transplant, you will then be allowed to return home to the care of your primary physician. You will be required to return to a local oncologist after transplantation so you can be monitored for late transplant complications including GVHD and infection. Thereafter you will be seen at NIH at 6, 9, 12, 18 and 24 months after your transplant and then every year following your transplant up to 5 years post-transplant, unless an earlier visit is required per the study doctors and more frequent monitoring if medically indicated. At each visit when you return to NIH, you will have a physical exam and blood draws (approximately 4-10 teaspoons of blood will be taken). During some visits you may have a bone marrow aspirate and biopsies, and other appropriate tests (for example: CT scans or other scans if you doctor feels it is indicated) to monitor disease status. Study-related medications will be provided by the NIH during your hospital stay and after you leave the NIH.

Post-transplant research tests

The skin and mouth are the two organs most commonly affected by chronic GVHD. It is important for you to know that these tests are being performed for research purposes to help us with our understanding of chronic GVHD. They would not routinely be performed unless they were needed to confirm the presence of chronic GVHD. These tests will be performed in all patients 60 days post-transplant and 6 months post-transplant. These tests may also be performed at the time of chronic GVHD diagnosis.

- Pulmonary function test – a noninvasive test to check how well the lungs work. During the test, you'll breathe in as much air as you can. Then, you'll quickly blow out as much air as you can through a tube connected to a machine called a spirometer.

- Echocardiogram or MUGA scan to evaluate your heart health
- Oral Photographs: We will take clinical photographs of your mouth and the surrounding area. Mirrors and retractors may be used to gently visualize areas of the mouth.
- Bone marrow aspiration and biopsy: Your pelvis will be numbed with a local anesthetic called lidocaine. A small cut will be made in the skin and a needle will be inserted into the pelvis. Liquid samples (aspiration) of the bone marrow will be removed through the needle. A small fragment of bone will also be removed with the needle. After the procedure, the biopsy site will be covered with a small bandage – stiches are not needed to close the small cut.
- Skin Biopsy: This is performed so that a piece of skin may be examined under the microscope to get a closer look at what is going on in your skin and for diagnostic purposes. After cleaning the skin with alcohol and/or another antiseptic, a local numbing medicine (Lidocaine with or without epinephrine)--similar to what a dentist injects to numb your gums--is injected into the planned biopsy site. A sharp instrument which looks like a miniature cookie-cutter is used to remove a round plug of skin about the size of a pencil eraser. The biopsy site may be left open or may be closed by putting in one or two stitches, and a small dressing is applied. Sometimes more than one such skin sample may be needed.
- You will be expected to keep the dressing over the biopsy site dry for 1 to 2 days. Thereafter, the dressing may be changed daily until the suture(s) are ready to come out, usually in 7 days. Depending on circumstances, the suture(s) may be removed by one of us, by your own doctor and/or your doctor's assistant. This biopsy is optional; you will be asked to sign a separate consent at the time of procedure(s).
- Oral mucosa biopsy: The procedure is done in a similar manner as a skin biopsy, except that a dressing cannot be applied, because it is not possible to keep the area dry enough to keep the dressing on. This biopsy is optional; you will be asked to sign a separate consent at the time of procedure(s).
- Collection of saliva (natural mouth fluid): Saliva will be collected by spitting into a clean plastic tube for 5 minutes at set times after transplant. We will use saliva samples to measure your salivary gland function and to study in our laboratory factors that may be associated with the development of GVHD including the types of protein in the mouth. This is a simple procedure that does not have any risks or discomforts. We will use saliva samples to study in our laboratory factors that may be associated with the development of GVHD including the types of bacteria that live in the mouth. We believe these studies will help us understand more about oral GVHD and lead to better treatments for this painful condition.
- Oral swab and plaque collection (natural mouth material): We will take swabs of your mouth and collect plaque from your teeth. We will not do any cutting or injections to collect these samples. We will rub a cotton swab over an area in your mouth. The plaque will be collected with a sterile swab/toothpick. The samples will be used to study the microbiome (normal bacteria found in your mouth) and other laboratory factors, such as genomic analysis, that may be associated with the development of GVHD.

- Collection of whole blood: Blood will be collected to perform genomic analysis on T-cells, a cell in your immune system so that we can learn more about how those cells work. No research bloods will be collected after relapse.
- Bone Density Scan (DEXA): This test measures the density of your bones (bone thickness). The scan checks for possible bone damage from your treatments.

Relapse/Progression of disease

If you relapse, we will monitor the status of your occurrence of GVHD. These evaluations can occur at NIH Clinical Center ,via telephone, or telemedicine visits. No research bloods or procedures will be done and treatment will be stopped after relapse or progression.

STANDARD OF CARE TREATMENT

Treatments covered under this study may include a single medication or a combination of medications, surgery or radiation to treat your cancer. These treatments will not be experimental. Your doctors will describe your treatment plan to you in detail before asking you to sign this consent form. You may be asked to sign a separate consent form for any treatment procedures not outlined in this consent.

BIRTH CONTROL

If you are a woman who is breast feeding or pregnant, you may not take part in the study because some of the medicines used on this study may be harmful to your baby or your unborn child. If you are a woman who can become pregnant, or are the partner of a woman who can become pregnant, you will need to practice an effective form of birth control while you are on study treatment. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

If you are a male, you should not father a child or donate sperm while you are on study treatment. You should practice abstinence, or two effective forms of birth control before starting study treatment and during study treatment.

Effective forms of birth control include:

- abstinence
- intrauterine device (IUD)
- hormonal [birth control pills, injections, or implants]
- tubal ligation
- vasectomy

REMOTE ASSESSMENTS

In the first quarter of 2020, a pandemic was announced for COVID-19 (Coronavirus Disease 2019) which is caused by the virus SARS-CoV-2. In light of the pandemic, tele-medicine has been used as an alternative way to perform assessments without having participants in clinical trials come to the clinic. Your study doctor may determine that the risks associated with you visiting the clinic during the COVID-19 pandemic may outweigh the benefit from seeing you in person at the clinic. Remote assessments may be performed at the discretion of your study doctor via phone, email, or

video chat to speak with you directly about the following: patient history, verbal exam, symptom reporting, and education.

RISKS OR DISCOMFORTS OF PARTICIPATION

Transplant risks

Risk of Death from Allogeneic SCT: Patients undergoing allogeneic SCT are at risk of dying

from the transplant procedure and its possible complications. This risk of death due to transplant related complications typically ranges between 15% and 40% in the course of two years post-transplant. The risk of death or other complications can vary greatly, depending on the age of the patient, other prior and current illnesses, functional status or other factors.

Other risks from allogeneic SCT include:

Veno-Occlusive Disease (VOD) - A severe liver complication known as VOD occurs in less than 5 percent of allogeneic transplants. VOD is a chemotherapy side effect that causes blood vessels in the liver to be blocked. Severe VOD can lead to liver failure and death.

Graft Rejection: There is a chance that you may reject your donor's stem cells. If that were to happen, you would most likely recover your own blood cells. However, there is the rare possibility that your own cells may not recover. This may result in prolonged low blood counts, which may result in infection or bleeding and may lead to death. In this event, we would attempt to support you with transfusions, growth factors and antibiotics until your own blood counts recover. A blood test will be performed at 14, 28, 60, and 100 days after your transplant to find out if your body has accepted the donor cells. If no donor cells can be found, then we will conclude that you rejected them. In that case, your blood counts will probably return to the same levels as before the transplant in about 2 to 3 weeks. You will receive the growth factor filgrastim to help the cells engraft. In the event that your cells do not engraft, we may ask your donor to donate more cells.

Graft-Versus-Host Disease (GVHD): You will be at risk for the development of GVHD for many years after transplantation. Acute GVHD usually occurs within 3 months after transplantation and typically affects the liver, intestines, and skin. Symptoms of skin GVHD may be as mild as a rash with itching, or as severe as blistering and loss of the skin. Symptoms of intestinal GVHD may be as mild as heartburn and mild diarrhea, or as severe as vomiting, cramping abdominal pain and bloody diarrhea. Liver GVHD may be as mild as slight disturbances in liver blood tests or as severe as jaundice (yellowing of the skin) and liver failure. Mild GVHD (skin rash only) can be treated with steroid creams that you apply on your skin.

Severe GVHD can be very dangerous and needs to be treated aggressively. Treatment of severe GVHD initially includes weakening of the immune system, usually with intravenous (I.V.) steroids. Weakening of the immune system increases the risk of infection.

A delayed form of GVHD, known as chronic GVHD, typically occurs between 3 and 12 months post-transplant. Some degree of chronic GVHD affects about half of patients after transplantation. It most commonly affects the skin, mouth, eyes, muscle, joints, liver and intestines, but it may also affect other organs such as the lungs, genitals and bone marrow.

Symptoms of chronic GVHD may include thickening of the skin, itching, decreased range of motion in the joints, dryness of the mouth and eyes, mouth pain and difficulties swallowing, loss

of appetite, weakness, hair loss, weight loss, liver damage (including yellowing of the skin), painful intercourse and lung damage leading to shortness of breath and cough. Patients with severe chronic GVHD are also at increased risk of infection and death. Chronic GVHD is also treated with drugs that weaken the immune system such as steroids. Taking steroids may increase your risk of infection. Treatments with steroids and other drugs are usually prolonged and last 3-5 years, but occasionally longer.

Late Transplant Complications: There are other potential complications that can occur long after transplantation. These complications could affect any organ in the body including the heart, lungs, kidneys, liver, muscles, and brain. Rarely, patients who receive an allogeneic SCT are at risk for developing a second cancer such as lymphoma, leukemia, lung cancer or other tumors.

Other complications are also possible following your transplant. The most common complications are infections. Because you will be receiving drugs (e.g. sirolimus) that weaken the immune system, you are at greater risk to develop infections from uncommon organisms. These infections can be life-threatening, and could cause death.

There is up to 40 percent chance of death from complications of conventional allogeneic bone marrow transplants. Although we will use new/unconventional ways to try to reduce these odds, it is possible that our approach may not work or that it may even increase the chances of death. There is also the risk of complications that cannot be predicted.

Procedure Risks

Stem Cell Infusion: The donor cells will be infused fresh or frozen with a chemical called DMSO to protect them from the effects of freezing. Patients receiving thawed cells often develop side effects from the DMSO. DMSO side effects may include fever and allergic reactions, such as skin rash, itching, difficulty breathing, and low blood pressure. These reactions are usually mild and temporary, and they can be easily treated with IV fluids and medications.

Bone Marrow Aspiration and Biopsy: This procedure usually causes only mild pain for a short time at the biopsy site. Very rarely, bleeding or an infection may occur at the biopsy site.

Blood Draws: 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, your red blood cell count may drop causing anemia. Anemia can cause a lack of energy and other symptoms. Transfusions of red blood cells are sometimes needed to treat anemia.

Central Venous Catheter: Side effects of placing a central venous line in your chest wall include bleeding, bruising, blood clots, or pain in the area of insertion. This line will be placed by physicians with experience in this procedure. These physicians will discuss the above risks at the time of the line insertion. Rarely, placement of a central venous catheter can result in a collapsed lung. If a collapsed lung occurs, it may require hospitalization and temporary insertion of a plastic tube in your chest to re-expand the lung.

Lumbar Puncture (Spinal Tap): Though lumbar punctures are generally recognized as safe, some risks may include pain or bleeding at the site of needle insertion (the low back), infection, and headache.

Skin Biopsies: Whenever possible, we will perform biopsies on covered areas of the body. There may be minor bleeding right after the procedure and this can easily be controlled by applying pressure on the spot for a few minutes. Rarely, a bruise might form and this usually heals on its own. Sometimes a small infection may occur at the biopsy site. This can usually be treated with topical antibiotics. On the very rare occasion that a larger or deeper infection occurs, oral antibiotics may be needed for 7-10 days. An infection can be recognized by redness, soreness, and pus at the site. It generally starts 2 days or more after the procedure and does not clear up in another couple of days. These biopsy/excision sites generally heal very well, leaving red, white, dark or skin-colored flat scars. Sometimes, the scar that forms may be a bit thicker than usual. Rarely, a keloid (large, painful or itchy scar) may form. Keloids are more likely to form on the chin, earlobes, chest and upper backs of Blacks and Asians between adolescence and the 30's.

Oral mucosa biopsy: There may be minor bleeding, bruising, numbness and slight swelling. There is also the possibility of infection. Mouth sores have occurred in some patients, but this is uncommon.

Echocardiogram (ECHO): An echocardiogram is an ultrasound to evaluate your heart structure and function. This test is very safe and is performed using a probe with gel placed on your chest.

Pulmonary (lung) function testing: These tests measure how well your lungs work. They are usually safe for most people. However, because the test may require you to breathe in and out quickly, you may feel dizzy. There's a small risk that you might faint. If you have asthma, this test could cause you to have an asthma attack. In very rare cases, pulmonary function tests may cause a collapsed lung. If you have asthma or feel lightheaded during the test, tell your doctor.

Urine Tests: There are no physical risks to collecting urine.

Radiation Risks

In order to measure any changes in your thymus, an important organ in your immune system, we plan to get CT scans. The measurement of these changes is one of the ways in which we evaluate how the study drug is working. If you need scans to monitor your disease (such as lymphoma patients who may otherwise need CT scans of the neck, chest, abdomen and pelvis), we would not do an extra CT scan just for this purpose. You may also receive radiation from MUGA and DEXA scans.

During your participation in this research study, you may be exposed to radiation from up to 6 CT scans, 1 MUGA scan, and 1 DEXA scan. The amount of radiation exposure you may receive from these procedures is equal to approximately 1.43 rem. If you are a patient with lymphoma, the amount of radiation exposure you may receive from these procedures is equal to approximately 8.27 rem. A rem is a unit of absorbed radiation.

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. The average person in the United States receives a radiation exposure of 0.3 rem per year from these sources. This type of radiation is called "background radiation." No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The scans that you may get in this study will expose you to the roughly the same amount of radiation as 4.8 years' worth of background radiation. Most of the time, this amount of extra

radiation is not harmful to you. However, scientists believe that being exposed to too much radiation can cause harmful side effects. This could include getting a new cancer. We estimate that this could happen in about 1 out of every 1000 people who get a very large amount of extra radiation.

For patients with lymphoma, the scans that you may get in this study will expose you to the roughly the same amount of radiation as 27.6 years' worth of background radiation. Being exposed to too much radiation can cause harmful side effects such as an increase in the risk of cancer. The risk depends on how much radiation you are exposed to. Please be aware that about 40 out of 100 people (40%) will get cancer during their lifeline, and 20 out of 100 (20%) will die from cancer. The risk of getting cancer from the radiation in this study is 0.8 out of 100 (0.8%) and of getting a fatal cancer is 0.4 out of 100 (0.4%).

Please tell your doctor if you have had any radiation exposure in the past year, either from other research studies or from medical tests or care, so we can make sure that you will not receive too much radiation. Radiation exposure includes x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body.

If you are pregnant you will not be permitted to participate in this research study. If you are breast feeding and the protocol involves injection of radioactive material you will not be permitted to participate. It is best to avoid radiation exposure to unborn or nursing infants since they are more sensitive to radiation than adults.

Risks from Chemotherapy

Induction Chemotherapy:

As described previously, the type of induction chemotherapy you will receive depends on the type of disease you have. Some patients will receive fludarabine, cyclophosphamide, etoposide, doxorubicin, vincristine, and prednisone (called: EPOCH-F), while others will receive fludarabine, cytarabine, and filgrastim (called: FLAG). In addition, some patients will receive rituximab. It is important for you to know that this type of induction chemotherapy is likely to reduce your white blood cells for many days. This will place you at increased risk of infection. Such infections can be very serious and may result in death. For this reason, if you develop a fever higher than 101° F, you must see your doctor immediately. If necessary, you will be treated with antibiotics. Also, this chemotherapy will likely cause your platelet count to fall.

This may place you at increased risk of bleeding. If your platelet count becomes dangerously low, you will receive platelet transfusions. The chemotherapy may also cause you to develop a low red blood cell count, called anemia. Anemia can cause a lack of energy and other symptoms. Transfusions of red blood cells are sometimes needed to treat anemia. The following are known specific risks of each drug used within the specific regimen that you will receive:

EPOCH-F (with or without rituximab):

Etoposide:

Likely	Less Likely	Rare:
• low blood counts • hair loss	• nausea and vomiting • diarrhea • mouth sores	• low blood pressure • shortness of breath • secondary leukemia (a different type of cancer)

Prednisone:

Likely:	Less Likely:	Rare:
• weight gain • sodium and water retention • mood changes • elevated blood sugar • increased risk of infection	• stomach or bowel ulcers • high blood pressure • diabetes • thinning of bones with greater risk of fracture (long term use) • puffing of the face (long term use) • acne • thinning of skin • muscle wasting	• none

Vincristine:

Likely:	Less Likely:	Rare:
• nerve damage resulting in a feeling of "pins and needles" in hands and feet • constipation • hair loss	• loss of reflexes (foot drop), • low blood counts • hoarseness and pain in the jaw	• paralytic ileus (bowel function completely stops), • water retention

C*yclophosphamide:*

Likely:	Less Likely:	Rare:
• low blood counts • hair loss	• nausea and vomiting, • painful and bloody urination • sterility • water retention	• heart damage • secondary leukemia (a different type of cancer) • skin rash

Doxorubicin:

Likely:	Less Likely:	Rare:
• low blood counts • hair loss • Urine colored red for a day or two after the doxorubicin infusion	• nausea and vomiting • diarrhea • mouth & throat sores	• heart damage • secondary leukemia (a different type of cancer) • tissue damage if the drug leaks from the vein into surrounding tissue • bleeding bowel or stomach

Fludarabine:

Likely:	Less Likely:	Rare:
• low blood counts • lowered level of immune cells • increased risk of infection	• nausea and vomiting • diarrhea • fever • mouth & throat sores • loss of appetite • swelling (edema) • skin rash • muscle aches • headache • agitation • hearing loss • fatigue • weakness • numbness / tingling ("pins and needles")	• GI bleeding • lung damage • kidney damage • severe neurologic (brain and/or spinal cord) toxicity has occurred after very high doses including: blindness, deterioration of mental status, and death

Rituximab:

Likely:	Less Likely:	Rare:
• mild infusion reactions (fever, chills, nausea)	• severe infusion / hypersensitivity reactions (e.g. lowering of blood pressure, shortness of breath or difficulty breathing)	• tumor lysis syndrome (metabolic complications) • severe skin reaction/rash, • kidney failure • death • chest pain • cardiac arrhythmias (heart beating irregularly) • some other viral infections may be worsened or reactivated from a "sleeping state" in patients taking rituximab

Filgrastim (G-CSF):

Likely:	Less Likely:	Rare:
• bone pain • reversible lab changes in your blood test results	• headache • pain at the needle site • fevers • tiredness	• filgrastim can cause rupture of the spleen, which can cause death

FLAG:

Fludarabine and Filgrastim
As above in EPOCH therapy.

Cytarabine (Ara-C):

Likely:	Less Likely:	Rare:
• low blood counts, • lowered level of immune cells • nausea and vomiting • mouth sores • hair loss	• diarrhea, • loss of appetite, • flu-like symptoms • fevers • liver damage • eye irritation	• loss of coordination or balance • sleepiness • speech difficulties • coma

Transplantation Chemotherapy:

The main side effect of fludarabine and cyclophosphamide at these doses is severe bone marrow and immune system weakening, which decreases the production of red blood cells, white blood cells, and platelets. The doses that will be used could cause longer than normal bone marrow weakening, if the transplanted stem cells were rejected. Until the transplanted stem cells start to produce adequate numbers of blood cells, you will be at significant risk for infections, bleeding and severe fatigue. These conditions will be treated with antibiotics and transfusions. Other potential side effects of fludarabine and cyclophosphamide are described above.

Risks of Graft-versus-Host Disease Prevention:

As described above, you will receive tacrolimus, methotrexate, and sirolimus.

Tacrolimus:

Likely:	**Less Likely:**	**Rare:**
• decrease in kidney function • headache • tremors* • high blood pressure • increased infection	• gum inflammation • seizures* • high blood potassium levels • nausea • diarrhea or constipation • loss of appetite • abdominal pain • insomnia • high blood sugar • increase in blood lipid levels, • lowering of body magnesium levels requiring supplementation • liver damage • numbness or tingling in hands or feet	• coma • delirium
*Because of the risk of seizures and decreased reflexes while taking this medicine, you should not drive a car while taking tacrolimus.		

Methotrexate:

Likely:	**Less Likely:**	**Rare:**
• delay in the return of blood cells after transplant	• mouth sores • minor liver damage	• nausea • vomiting • diarrhea

Sirolimus:

Likely:	Less Likely:	Rare:
• your infection risk is likely increased. Because sirolimus as an immune suppression drug, it is likely the risk for some infections may be increased.	• diarrhea • nausea • damage to the liver • low blood counts • very high levels of fats (triglycerides) • increased cholesterol (increased lipid blood levels) • mouth ulcers • headache • increased risk of infection • red blood cell lysis with associated reduced kidney function	• severe swelling of the pancreas • secondary cancers (a different type of cancer)

Risks of Palifermin: (Kepivance ®)

Likely:	Less Likely:	Rare:
• skin reactions (rash, irritation, redness, swelling, itching) • fever • tongue thickening or discoloration • visible water retention	• high blood pressure • numbness • abnormal sensations of the skin • joint pain • change in taste • tingling, numbness, prickling, or burning sensation around the mouth or on the skin	• rash; hives; difficulty breathing • tightness in the chest • swelling of the mouth, face, lips, or tongue

Other Medications

You will routinely receive several other drugs to prevent or treat various infections and other transplant-related complications. The most common medications used and their common side effects are listed as follows:

Ursodeoxycholic acid, also known as ursodiol, can cause nausea, vomiting, “heartburn”, a metallic taste, abdominal pain, an inflamed gallbladder, constipation, mouth pain, flatulence, diarrhea, itching, rash, dry skin, hives, headache, fatigue, anxiety, depression, and sleep disorders. Less common side effects include sweating, thinning of hair, back pain, muscle and joint pains, runny noses, and cough.

Mesna is a drug given with cyclophosphamide during the conditioning regimen to prevent bladder injury, and side effects may include: nausea, vomiting, and diarrhea.

Furosemide is a drug given with the cyclophosphamide and IV fluids in order to prevent fluid buildup, as well as to prevent bladder injury. Side effects of furosemide may include low potassium and low magnesium levels, loss of appetite and low blood pressure. Serious side effects are rare, but include low platelets, anaphylaxis and skin rashes.

Diphenhydramine may cause tiredness, dizziness, upset stomach, disturbed coordination, dry mouth, flushing, or difficulty urinating.

Acyclovir can cause nausea, vomiting, headache, dizziness, abdominal pain, bone pain, allergic reactions, mild liver inflammation, kidney injury, and abnormal nervous system function.

Fluconazole can cause nausea, vomiting, headache, skin rash, abdominal pain, and diarrhea. Rare but sometimes serious liver toxicity has also been reported. Fluconazole can increase the blood levels of other drugs, which can increase their effectiveness and/or their side effects.

Trimethoprim/sulfamethoxazole (Bactrim) may cause nausea, vomiting, loss of appetite, allergic skin rashes, and suppression of bone marrow function. Rare but severe reactions may affect the skin and bone marrow; these have sometimes been fatal.

Reproductive Risks: This treatment is likely to result in sterility (the inability to produce children). However, we cannot predict for certain that you will become sterile during this treatment; therefore you will be asked to use birth control while on the study as discussed above.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

The chemotherapy you receive may cause improvement in your cancer, although it is not likely to result in a cure by itself. The allogeneic SCT may improve the chance that your disease will enter into a long remission and possibly be cured. However, you should understand that this cannot be guaranteed. Your participation in this study may contribute to understanding and developing new ways of using allogeneic SCT for the treatment of cancer.

ALTERNATIVE APPROACHES OR TREATMENTS

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

To be eligible for this study, you must have already received the standard treatment for your disease, but there are other options other than participating on this trial:

- You may consider other treatments such as other forms of chemotherapy, radiation, surgery, or immune therapies. In some cases, you may be eligible for an autologous bone marrow or stem cell transplant, in which your own stem cells are returned to your body following high dose chemotherapy treatment.
- Taking part in another research study
- Instead of participating in a research study such as this, you may also be eligible to receive a standard allogeneic stem cell transplant with high dose chemotherapy and/or radiation therapy to completely wipe out your bone marrow before donor cells are transplanted.

- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.
- Another option is not to receive any further treatment at all.

You should discuss with your referring doctor and your doctors at the NCI whether or not any of these other treatments might be a reasonable choice for your disease.

STOPPING THERAPY

Your doctor may decide to stop your therapy for the following reasons:

- if s/he believes that it is in your best interest
- if your disease comes back before you have had your transplant
- if you do not meet the transplant eligibility criteria after you have completed induction therapy

In this case, you will be informed of the reason therapy is being stopped.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases cannot be recalled and destroyed.

CONFLICT OF INTEREST

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a Protocol Review Guide. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines but they do not need to report their personal finances to the NIH.

Members of the research team working on this study may have up to $15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.

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.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. The amount and form of these payments are determined by the NCI Travel and Lodging Reimbursement Policy. You will be given a summary of the policy which provides more information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- If some tests and procedures are performed outside the NIH Clinical Center, you may have to pay for these costs 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 NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The study Sponsor (Center for Clinical Research) or their agent(s)
- Qualified representatives from Swedish Orphan Biovitrum (Sobi), the pharmaceutical company who produces palifermin.

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.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH 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 NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

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, Steven Pavletic, MD, 240-760-6174, pavletis@mail.nih.gov. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

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

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness should sign below if either:

1. **A short form consent process has been used to enroll a non-English speaking subject or**
2. **An oral presentation of the full consent has been used to enroll a blind or illiterate subject**

Signature of Witness	Print Name of Witness	Date

NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.