WVU1909

UNRELATED UMBILICAL CORD BLOOD (UCB) TRANSPLANTATION

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WVU 1909 Consent Form Version:04OCT2017

Principal Investigator: Michael Craig, MD

Department: Medicine- Hematology/Oncology

Study Title:
WVU 1909: Unrelated Umbilical Cord Blood (UCB) Transplantation

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Sponsor

Sponsor-Investigator: Michael Craig, MD
Mary Babb Randolph Cancer Center of West Virginia University

Contact Person
In the event you experience any side effects or injury related to this research, you should contact Dr. Craig at (304)598-4500.(After hours contact the BMT/Hem Malignancy physician on call at (304)598-4000.)

For more information about this research and about research –related risks or injury, you can contact Dr. Craig at (304)598-4500

For more information regarding your rights as a research subject, you can contact the Office of Research Compliance at 304/293-7073.

Introduction

You, _____ have been asked to voluntarily participate in this research study, which has been explained to you by _____. This study is being conducted by Principal Investigator Michael Craig, MD in the Department of Medicine at West Virginia University.

Purpose of the Study

You have been asked to participate in this study because you have a hematologic malignancy (a disease of your bone marrow or lymph nodes) that is not curable with standard therapy. Your disease may be treated with chemotherapy, radiation and hematopoietic progenitor cell (HPC – the primitive cells in the blood and bone marrow that can restore the bone marrow) transplant.

You unfortunately do not have a matched adult donor to use as your HPC cell source or your disease has progressed and time does not allow a long search for a matched adult donor. However, you do have a matched umbilical cord blood HPC source available. Currently umbilical cord HPC transplants are not standard of care in the adult patient. This is currently being studied as a curative option in patients with a life threatening hematologic disease with no standard HPC donor source.

The purpose of this study is to assess the engraftment rate, safety, disease progression, survival and incidence of complications (infections, Graft versus Host Disease) when using cord blood as a source of HPC in an adult/older adolescent.

Approximately 40 patients are expected to participate in this study at West Virginia University Hospital.

Description of Procedures

Before your treatment begins you will have a detailed medical history taken and undergo a physical examination including blood tests and tests of your heart and lungs to determine if it is safe for you to undergo umbilical cord Hematopoietic Progenitor Cell (HPC) transplantation. You will also have tests to evaluate your disease. You will have about 6 – 8 teaspoons of blood drawn. This amount is equal to about 1/10th of the amount taken if you were to donate a unit of blood. If your tests show that it is safe for you to undergo a HPC transplant then the following events will take place during the course of your treatment.

You will be hospitalized for approximately 4-6 weeks or longer if necessary. You will need to remain in the Morgantown area or nearby for approximately 100 days following your transplant in order for your condition to be monitored. After Day 100, you will need to make frequent visits back to Morgantown to see your transplant doctor for continued close medical supervision for at least one year following your transplant.

Before your treatment begins, you will have central venous catheters (a small, flexible plastic tube inserted into a large vein above the heart, through which drugs and blood products can be given and samples withdrawn painlessly) placed.

The source of your HPC will be from an unrelated donor's umbilical cord, collected at the time of their birth.

Your treatment will begin 6 days before you are scheduled to receive the donor's cord stem cells with the start of a conditioning regimen.

Conditioning Regimen:

The conditioning regimen is a combination of chemotherapy and/or radiation given to patients before their donor cells are infused. This treatment allows donor cells to engraft (take hold) and

start growing in your bone marrow. This treatment also helps to kill cancer cells that might not be detected.

Different chemotherapy drugs and/or radiation can be used as part of the conditioning regimen and the combination of drugs and radiation and the dose used can have different strengths that can be called treatment "intensity".

High intensity treatments are known as myeloablative regimens. These treatments destroy cancer cells because they use very high amounts of chemotherapy or radiation. These high intensity treatments often times have more side effects during and after transplant.

Lower or "reduced" intensity treatment before transplant can have fewer serious problems from the chemotherapy or radiation. The killing of cancer cells may be lower but studies have shown that immune cells given in the transplant can help destroy any remaining cancer cells. Reduced intensity regimens are often used for people that may not be able to tolerate high dose chemotherapy or radiation due to their age or other medical problems and has shown to be effective in certain types of disease.

Your physician will decide which conditioning regimen (high intensity or reduced intensity) is best for you. It will be based on several factors such as your age, your medical condition at the time of transplant and your disease.

You will receive one of these two conditioning regimens:

High Intensity (myeloablative) Conditioning Regimen:

Fludarabine -Days 1,2,3 and 4 by intravenous (IV) infusion

Busulfan - Days 1,2,3 and 4 by IV infusion

Total Body Irradiation-on Day 6 you will receive one treatment

Anti-thymocyte Globulin (ATG)-Optional - on Days 3, 4 and 5 you may receive this drug as an IV infusion. This is optional and your physician will decide if this is best for you.

Cord Blood Transplant – On Day 7 you will receive your donor cord blood stem cells by IV infusion.

Reduced Intensity Conditioning Regimen:

Fludarabine -Days 1,2, 3, 4 and 5 by intravenous (IV) infusion

Cyclophosphamide - Day 1 by IV infusion

Total Body Irradiation – on Day 6 you will receive one treatment

Anti-thymocyte Globulin (ATG)- Optional - on Days 3,4,5 you may receive this drug as an IV infusion. This is optional and your physician will decide if this is best for you.

Cord Blood Transplant –On Day 7 you will receive your donor cord blood stem cells by IV infusion.

In order to get a high enough stem cell dose for your transplant, you most likely receive cells from two different cord bloods. This is based on factors such as size of the stem cell dose of the cord bloods that best match you and on your size (height/weight).

It should take approximately 2-4 weeks following treatment for your donor's cells to engraft (take hold) and begin to make adequate white blood cells. It may take longer than this for your platelet count to normalize without platelet transfusions. During this time, you will be monitored with blood tests to check your blood counts and the levels of other chemicals and drugs in your body and to detect infection. You will have approximately 3 teaspoons of blood drawn daily as standard care.

Follow up procedures/testing and supportive care after you receive your donor cord blood stem cells are standard of care for stem cell transplant patients

You will receive supportive care with platelet and red blood cell transfusions, and anti-microbial (medicines to protect you against microorganisms such as bacteria, fungus and viruses). You may also receive immune globulins (proteins that help protect the body from infection).

In a continued attempt to prevent graft-versus-host disease, you will be placed on medications to suppress your immune response. These medications will be continued for six to twelve months. You will need to continue taking these medicines at home after you are discharged from the hospital.

You will be discharged from the hospital following your transplant when your blood counts recover, and you are able to eat and drink adequately and are having no fevers. When you are discharged from the hospital, it is important for you to understand that you will need to have a caregiver to stay with you at all times until your transplant physician tells you that it is safe for you to stay alone.

Around day 30 after your transplant, your physician will do a blood test to see if your donor's hematopoietic progenitor cells (HPC) have engrafted (taken hold) adequately. The amount of blood required for this blood test is approximately 3 teaspoons. Additional testing after your transplant, such as additional blood testing, x-rays, CAT and PET scans, and pulmonary testing may be performed as your medical condition requires and your physician will determine the appropriate testing that is necessary.

During the course of your treatment appropriate medical care will be available and referrals to specialized physicians will be made if needed.

At the time you are well enough to return home, you will be followed as your condition requires by your local physician for lab and physical exams. You will be required to return to Cancer Center for follow-up by your transplant doctor. The frequency of the visits will be determined by your doctor and will be based on your medical condition. You will need to return on or around Day 180 (6 months) post stem cell transplant for the final required treatment visit for this study. After Day 180, you will be followed and monitored per the standard WVUH BMT operating procedures.

Risks and Discomforts
Treatments often have side effects. The treatments used in this protocol may cause all, some, or none of the side effects listed. In addition, there is always the risk of very uncommon or previously unknown side effects occurring.

Cyclophosphamide (Cytoxan)

Likely Side Effects(May happen in more than 20% of patients): may cause nausea and vomiting, diarrhea, loss of appetite, hair loss, irregular menstrual periods, a lowering of white blood cell and platelet counts (which could cause an increased risk of infection, easy bruising and bleeding), anemia, headache, dizziness and fluid retention.

Less likely(may happen in less than 20% of patients): Bleeding/irritation of the bladder, inflammation of the heart muscle (heart failure), shortness of breath. These side effects are usually temporary and may be lessened by giving fluids to irrigate your bladder and by monitoring your heart function closely while receiving this drug

In rare cases (less than 2% of patients): it may cause allergic reaction, lung fibrosis and serious skin rashes. This drug has been reported to cause a second malignancy of acute leukemia.

Fludarabine

Likely Side Effects (May happen in more than 20% of patients) This therapy will cause the lowering of your white blood cell counts (making you susceptible to infections), platelets (making you susceptible to bleeding), and red blood cell count (causing anemia and making you tired). Nausea, vomiting, loss of appetite and diarrhea, reversible hair loss and mouth sores/ulcers.

Less likely (May happen in less than 20% of patients): events include headache, skin rash, fever, numbness in the extremities, sleepiness, weakness and visual changes.

Rare events(less than 2% of patients): such as coma, cough, inflammation of the lung, pneumonia and skin rash can occur.

Busulfan-

Likely Side Effects (May happen in more than 20% of patients) This therapy will cause the lowering of your white blood cell counts (making you susceptible to infections), platelets (making you susceptible to bleeding), and red blood cell count (causing anemia and making you tired). Nausea, vomiting, loss of appetite, heartburn, diarrhea, constipation, abdominal discomfort, mouth sores/ulcers, dizziness, fluid retention, headache, insomnia, runny nose, skin rashes, irregular or no menstrual cycles, fast heartbeat.

Less likely (May happen in less than 20% of patients):events include cough, Veno-occlusive disease (form of liver damage), high blood pressure, low blood pressure, high levels of magnesium and phosphorus in the blood, high blood sugar levels, seizures, inability to have children.

Rare events(less than 2% of patients) such as cataracts and scarring of the lungs can occur.

***Anti-thymocyte globulin* (ATG)**– May cause allergic reactions, anaphylaxis, serum sickness, rash, fevers/chills, lowering of blood counts.

Total Body Irradiation (TBI) – May cause nausea, vomiting and feeling tired. It may also cause reddening of your skin, and possible scarring of your liver and lungs. A Radiation Oncologist will see you in consultation and he or she will explain in detail the risks, benefits and side effects of radiation. You may be asked to sign a separate consent form for this part of the treatment.

Risks Related to the Transplant Procedure: The following risks are part of the transplant process and not connected to any one medication or the transplanted donor cells.

Bleeding: Platelets help your blood to clot. When you have low amounts of platelets, you may have bleeding problems. When your new bone marrow starts to grow, your platelets will increase and your blood will start to clot normally again.

Bleeding problems can range from minor bleeding, such as nosebleeds or bruising, to more serious bleeding in your brain and lungs. Serious bleeding can be very dangerous and can happen if your platelet levels stay low. Usually, we can prevent major bleeding problems with transfusions of platelets. However, if your body does not respond well to transfused platelets, you may be at serious risk for bleeding.

Slow Recovery of Blood Counts: The red blood cells, white blood cells and platelets can be slow to recover after a cord blood transplant. Until your blood counts recover you will need blood and platelet transfusions and will be at an increased risk for bleeding and infections.

Infections: Full and complete recovery of your immune system may take months. During this time you are at an increased risk of infections some of which can be serious. You will be prescribed certain drugs to reduce the chance of these infections. However, these treatments do not always work. If you have an infection you may have to stay in the hospital longer or be re-hospitalized after transplant. Although most infections can be treated, some infections may result in death.

Graft Failure: The cord blood stem cells (" the graft") may fail to grow in your body. If the graft failure occurs this may result in low blood counts for a long period of time. The chance of graft failure may be 10-15%. If your counts do not recover, you may need to receive a second transplant. Graft failure can be fatal.

Veno-occlusive Disease (VOD): High dose chemotherapy, radiation therapy and medications used to prevent GVHD can cause veno-occlusive disease (VOD). VOD causes severe damage to the liver. Symptoms include jaundice (yellowing of the skin and eyes), weight gain, and extra fluid build-up in the belly (abdominal cavity) and other parts of the body. We can usually manage veno-occlusive disease very well, to the point where it goes away. However, complications can happen with VOD that may put your life in danger.

Mouth Sores and Diarrhea: The large doses of chemotherapy and radiation cause irritation in the lining of the mouth and intestines. This can result in painful mouth sores and diarrhea. If you have severe mouth sores, we will give you medicine to help control the pain. If your mouth sores are very bad, you may not be able to eat normally until the sores are healed. Mouth sores get better when your white blood count starts to rise, and your donor cells start to grow (also called engraftment).

Capillary Leak Syndrome: This can happen from your chemotherapy and radiation treatments. The blood vessels may become 'leaky' and fluid enters your abdomen, lungs, and other tissues. You may gain water weight and not go to the bathroom as often as you normally do. Capillary leak syndrome can be difficult to manage if extra fluid enters your lungs and makes it hard to breathe. You may die if fluid continues to build up in your lungs.

Unexpected Organ Damage and Other Side Effects: You might have unexpected, life-threatening heart, lung, kidney, or liver damage as a result of your transplant. High doses of

chemotherapy and radiation can cause very bad lung damage that may not get better with time or medications. If this happens, you may need to use oxygen or even a respirator. The lung damage may get worse and be life-threatening. Rarely, multiple organ failure (such as lung and kidney failure) can happen, which can lead to death.

Graft-versus-Host Disease – You will be treated with medications to prevent and to help control GVHD if it develops. However, these medications may not prevent or control the GVHD. If you develop GVHD, it may range from mild to severe and it can be fatal in some cases. The GVHD itself may cause you to have rash, blistering, swelling, peeling and breakdown of your skin, increased nausea, vomiting and diarrhea, decreased liver function or liver failure. Additionally, the medications themselves may cause side effects such as, pain in your hands and feet, excessive hair growth, nausea, tremor, seizures, tenderness, swelling or bleeding of the gum, decreased magnesium in your blood, increase in blood tests that measure your liver function, increased risk of infections, high blood pressure, retention of fluid, kidney damage, increased appetite, weight gain, excessive production of stomach acid, weakening of your bones, depression, cataracts, acne, allergic reaction (rash, itching, hives, swelling, shortness of breath), inflammation of your joints, chills, and decreased white blood cell counts.

Fluid Build-up: We will give you intravenous (IV) fluids during the transplant process and it can be hard for your body to eliminate this fluid. We will also give you Furosemide, which is a medication that can help your body get rid of the extra fluid. One risk of Furosamide is hearing loss. Some side effects may be loss of body chemicals such as potassium and sodium.

Late Effects: You may have side effects that happen a few months to many years after your transplant. You may have problems with your thyroid gland that require you to take thyroid medication.

- You may get cataracts earlier in life compared to a person who has not had a transplant. If you develop cataracts (cloudiness in the eyes) they may need treatment.
- Your kidneys could be affected and cause anemia (low red blood cell count) or high blood pressure.
- You may develop a second cancer as a result of the chemotherapy, radiation and/or underlying disease. If secondary cancers happen they generally do not develop until 5 to15 years after your transplant.
- We do not know the long-term effects of transplant on your heart, lungs and brain

This treatment has a risk of death that may be as high as 40% depending on individual patient related factors. Your doctor will be checking you closely to see if any of these problems or side effects are occurring.

Withdrawal from this treatment after chemotherapy and TBI have started and before your cord cells have been transplanted may result in your death.

Additional Risks Related to Supportive Care Procedures:

Transfusion of Blood Products – The therapy used for the treatment of your disease will cause your blood counts to be decreased. It is likely that you will require the transfusion of blood products until your blood counts return to a safe level. There are risks associated with receiving blood products. These include the risk of transfusion reaction (itching, hives, rash, chills, fever, shortness of breath, the destruction of red blood cells and blood in your urine), and exposure to infectious diseases such as hepatitis (liver infection) and Human Immunodeficiency Virus (HIV), the virus that causes AIDS.

Infusion of Umbilical HPC - Risks associated with the infusion of your donor's umbilical cord stem cells are the same as those associated with the transfusion of blood products. Preservatives may have been added to help store the stem cells, additional risks may occur from the preservative used. These risks include nausea, vomiting, reddening of your skin (flushing) shortness of breath, hives low blood pressure and a peculiar body odor somewhat similar to garlic.

Central Venous Catheter Placement - May result in bleeding, infection or pain at the site of entry or under the skin. There is also a small risk of collapsing the lung, requiring placement of a tube to re-expand the lung. You will be asked to sign a separate consent for this procedure.

Prevention and Treatment of Infections – The drugs typically used to prevent and treat viral, fungal and bacterial infections found in transplant patients may cause rash, itching, fever, chills, shortness of breath, difficulty breathing, swelling, decreased kidney function, increases in the blood tests that measure your liver function, nausea, vomiting, diarrhea, loss of appetite, a decrease in your blood counts, abdominal discomfort and, peripheral neuropathy (disturbances in the function of the brain or spinal cord that may affect the nerves and muscles of the body).

Cancer chemotherapy drugs and TBI will make most people sterile (incapable of having children). The long-term effects on reproductive cells (sperm or ova) in the human body are unknown. Chemotherapy may cause lasting effects on the reproductive potential of both men and women. You understand that you should discuss options to store your reproductive cells with your physician before receiving this treatment.

This treatment may involve risks to the unborn child. If you are pregnant or breast-feeding, you will not be permitted to receive treatment. If you are a woman who may become pregnant, you will not be allowed to undergo treatment until you have had a pregnancy test and the test indicates that you are not pregnant. If you are pregnant, alternative treatment will be discussed. You must use a medically approved method of birth control while receiving this therapy.

Alternatives
You do not have to participate in this study. Alternatives that could be considered in your case include:

- Taking part in another study
- Receiving other treatment or combination of treatments
- Receiving no further treatment
- Receiving comfort care (palliative care). This treatment helps reduce the symptoms associated with cancer (such as pain, fatigue, appetite problems). It does not treat the cancer directly, but tries to improve the way that you feel and keep you active.

Benefits

The potential benefit of this treatment is to help control/treat your disease. It is unknown whether you will derive any personal benefits from receiving this treatment. Information from this study may help you and/or other people with the same disease get better care in the future.

Financial Considerations

There are no special fees for participating in this study.

Side effects associated with the treatment of your disease may result in prolonged hospitalization, frequent laboratory work and the use of medication and/or procedures to treat side effects and that these may result in added cost to you. Cost associated with this treatment will be negotiated before you begin treatment and will be discussed with you and will be paid by a third party payer, private, private fundraisers, trust funds or you directly.

Voluntary Compensation

If you become sick or are injured as a result of this research, treatment will be available. The investigator, West Virginia University or its associated affiliates will not voluntarily provide compensation for your injuries.

Confidentiality

Any information about you that is obtained as a result of your participation in this research will be kept as confidential as legally possible. Your research records and test results, just like hospital records, may be subpoenaed by court order or may be inspected by federal regulatory authorities (including the FDA if applicable) or the West Virginia University Institutional Review Board without your additional consent.

In addition, there are certain instances where the researcher is legally required to give information to the appropriate authorities. These would include mandatory reporting of infectious diseases, mandatory reporting of information about behavior that is imminently dangerous to you or to others, such as suicide, child abuse, etc.

In any publications that result from this research, neither your name nor any information from which you might be identified will be published without your consent.

You can decide to sign or not to sign this authorization section. However, if you choose not to sign this authorization, you will not be able to take part in the research study. Whatever choice you make about this research study, it will not have an effect on your access to medical care.

Since you are receiving HPC from an unrelated cord blood, information about your disease, treatment, complication and progress after transplant will be released to the NMDP/CIBMTR (transplant data registries). You will sign a separate consent form for this.

Persons/Organizations providing the information: West Virginia University Hospitals, applicable health information from your referring physicians, hospitals and yourself (patient).

Persons/Organizations receiving the information:

- The research site(s) carrying out this study. This includes UHA or UHA Affiliated, WVU, WVU Hospitals. It also includes each site´s research staff and medical staff.
- Health care providers who provide services to you as part of this research study.
- Laboratories and other people and groups that look into your health information as part of this study in agreement with the study protocol.
- The United States Department of Health and Human Services (which includes the National Institutes of Health, Food and Drug Administration (FDA)) and other groups that have the right to use the information as required by law.
- The members and staff of WVU Institutional Review Board (IRB) that oversees this research study.
- West Virginia University Office of Research Compliance and Office of Sponsored Programs.
- West Virginia University Clinical Trials Research Unit.

The following information will be used: Information from your existing medical records and new information about you that is created or collected during the study such as: history and physicals, clinic visit notes, nursing and staff notes, laboratory results, pathology results, x-rays, EKG results, demographic data, pulmonary tests, imaging scans and study forms.

The information is being disclosed for the following reasons:

- Publication of study results (without identifying you)
- Review of your data for quality assurance purposes
- Other research purposes such as reviewing the safety or effectiveness of the study drug and other products or therapies; conducting performance reviews of the study drug; evaluating other products or therapies for patients; developing a better understanding of disease; improving the design of future clinical trials

You may cancel this authorization at any time by writing to the Principal Investigator:
Michael Craig, MD
Mary Babb Randolph Cancer Center – 1 Medical Center Drive

Morgantown, WV 26506-8110 Phone 304-598-4520

If you cancel this authorization, any information that was collected already for this study cannot be withdrawn. Once information is disclosed, according to this authorization the recipient may redisclose it and then the information may no longer be protected by federal privacy regulations.

You have a right to see and make copies of your medical records. You will not be able to see or copy your records related to the study until all work related to the study is completed. At that time you may ask to see the study doctor´s files related to your participation in the study and have the study doctor correct any information about you that is wrong.

This authorization will not expire unless you cancel it.

Voluntary Participation

Participation in this study is voluntary. You are free to withdraw your consent to participate in this study and such refusal to participate will not affect your future care. Withdrawal of consent after chemotherapy/TBI but before your HPC transplant, may result in your death.

In the event that new information becomes available that may affect your willingness to continue, this information will be given to you so that you may make an informed decision about your participation.

You have been given the opportunity to ask questions about the research, and you have received answers concerning areas I did not understand.

Signatures

Upon signing this form, you will receive a copy.
I willingly consent to participate in this research.

Signature of Subject or Subjects Legal Representative	Printed Name	Date	Time

The participant has had the opportunity to have questions addressed. The participant willingly agrees to be in the study.

Signature of Investigator or	Printed Name	Date	Time

Co - Investigator

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Subject's Initials_____

Date_____