Patient Informed Consent Template for the BMT CTN 1502 Study

Optimizing Haploidentical Aplastic Anemia Transplantation

Your Name: _____

Study Title: Optimizing **H**aploidentical **A**plastic Ane**m**ia Trans**p**lantation (CHAMP)

Protocol: BMT CTN #1502

Co-Investigator: Amy E. DeZern, M.D., M.H.S.
Division of Hematologic Malignancies
1650 Orleans Street, CRBI Room 3M87
Baltimore, MD 21287-0013
(O) 410-502-7208
(F) 410-614-7279
adezern1@jhmi.edu

Co-Investigator: Michael A. Pulsipher, M.D.
Division of Pediatrics, USC Keck School of Medicine
Children's Hospital Los Angeles
4650 Sunset Blvd, MS#54
Los Angeles, CA 90027
(O) 323-361-2546
(F) 323-361-8068
mpulsipher@chla.usc.edu

Principal Investigator: *Insert local PI information*

Sponsor: The National Institutes of Health (NIH) is sponsoring this study by providing financial support through the Blood and Marrow Transplant Clinical Trials Network (BMT CTN).

1. Introduction

We invite you to join this clinical trial, also known as a research study. You're being asked to join because you:

- Have a diagnosis of severe aplastic anemia (SAA), and
- Your SAA can be treated with an **allogeneic transplant.** You don't have a completely matched **related donor**, but you do have a half-matched family (**haploidentical**) bone marrow donor.

This study will take at least 3 years and will include 30 participants. Your participation will last for **1 year** after your transplant.

This Consent Form will tell you about the purpose of the study, the possible risks and benefits, other options available to you, and your rights as a participant in the study.

Everyone who takes part in research at [insert facility name] should know that:

- Being in any research study is voluntary.
- You may or may not benefit from being in the study. Knowledge we gain from this study may benefit others.
- If you join the study, you can quit the study at any time.
- If you decide to quit the study, it will not affect your care at [insert name of facility or institution].
- Please ask the study staff questions about anything that you do not understand, or if you would like to have more information.
- You can ask questions now or any time during the study.
- Please take the time you need to talk about the study with your doctor, study staff, and your family and friends. It is your decision to be in the study. If you decide to join, please sign and date the end of the Consent Form.

You and your doctor will discuss other treatment choices if you do not want to participate in this study.

2. Study Background

The National Institutes of Health (NIH), through the Blood and Marrow Transplant Clinical Trials Network (BMT CTN), is providing staff support and money for this research study. The BMT CTN and the NIH will make decisions together about how to manage the study.

An **allogeneic transplant** uses blood-making cells from a **related donor** (family member) or an **unrelated donor** (not a family member) to replace your diseased blood cells. Before your transplant, you will get chemotherapy with radiation to destroy the diseased cells.

After chemotherapy, the healthy cells from your donor are given to you. The new cells go into your bloodstream through an intravenous (IV) catheter (or tube). It's just like getting blood or medicine through an IV. The donor cells find their way into your marrow where most often they grow and start to make healthy new red blood cells, white blood cells, and platelets.

For this study, the cells used for your transplant will come from **bone marrow** (related donor), which is soft, spongy tissue inside of bones. The bone marrow will come from a half-matched (haploidentical) family member such as a sister, brother, child or parent. This means that you and the donor have one set of genes (out of two possible) that are the same, or are half-matched. This is called a **haploidentical transplant**. 'Haplo' means half.

3. Study Purpose

We invite you to take part in this study because you have severe aplastic anemia (SAA) and an allogeneic transplant is a treatment option for you. We're doing this study to learn how well SAA patients do with transplants that use haploidentical bone marrow.

4. Rights to Ask Questions and/or Withdraw

You have the right to ask questions about the study at any time. If you have questions about your rights as a participant or if you want to leave the study, please contact:

[insert contact info]

Being in this study is voluntary. You can choose not to be in this study or leave this study at any time. If you choose not to take part or leave this study, it will not affect your regular medical care in any way.

Your study doctor and study staff will be available to answer any questions that you may have about taking part in or leaving this study.

5. Study Treatment and Tests

If you join the study, we will check your health before you start treatment, while you receive treatment, and for 1 year after your transplant.

Before Your Treatment

You will need to have several check-ups and tests to see if you can be in the study. These check-ups and tests are part of your regular care. They would be done even if you were not part of this study. These tests include:

- Medical history
- Physical exam, height, and weight
- Blood and urine tests
- Heart function tests

- Lung (pulmonary) function tests; for children, pulse oximetry test to measure how much oxygen is in your blood.
- Bone marrow tests. These tests are called aspirates or biopsies. Samples of your marrow will be taken from your hip bone with a large needle.
- A pregnancy test if you are a woman and able to have children (if you are pregnant, you will not be able to join this study).

During Your Treatment

If the check-ups and tests show that you can be in the study, you'll get a bone marrow transplant from a half-matched (haplo-identical) family member.

Before Your Transplant:

The conditioning regimen is the combination of chemotherapy drugs (chemo) and radiation you'll receive before you get your donor cells. This helps the donor cells start to grow and make new cells in your bone marrow (engraft).

A common side effect of allogeneic transplant is Graft versus Host Disease (GVHD). It's a medical condition that can be very serious (see Risks and Toxicities Related to Transplant under **Section 6: Risks and Discomfort**).

GVHD happens because of differences in your immune cells (host) and your donor's immune cells (graft). The donor cells might see your cells as foreign and attack them, causing GVHD to happen. Your doctor will give you drugs to help prevent GVHD from happening.

Your doctor will use the following drugs and radiation to prepare your body for transplant:

- **Thymoglobulin®, also known as anti-thymocyte globulin, rabbit ATG and rATG** (helps the donor cells engraft in your body and is also a GVHD prevention drug)
- **Fludarabine** and **Cyclophosphamide** (chemotherapy drugs)
- **Total body irradiation, TBI** (radiation therapy given to the whole body to help weaken your immune system and prevent rejection of transplanted stem cells)

- We'll give you Thymoglobulin® each day for 3 days, starting 9 days before your transplant (Day -9 through Day -7).
- Then we'll give you Fludarabine each day for 5 days, starting 6 days before your transplant (Day -6 through Day -2).
- You'll also get Cyclophosphamide for 2 days, starting 6 days before your transplant (Day -6 and Day -5).
- Last, you'll get a low dose of TBI the day before your transplant (Day -1).

After your transplant, you'll also get drugs to help prevent GVHD:

- You'll get **Cyclophosphamide** for 2 days, starting 3 days after your transplant (Day +3 and Day +4). Your doctor will give you this drug in your vein (IV).
- We'll give you **Tacrolimus** daily starting 5 days after your transplant (Day +5). Your doctor will either give you this drug in your vein (IV) or you will take a pill.
- Then we'll give you **Mycophenolate mofetil** (MMF) daily starting 5 days after your transplant (Day +5). Your doctor will either give you this drug in your vein (IV) or you will take a pill.
- You will continue to take Tacrolimus (or a similar drug called Cyclosporine) for about 6 to 12 months, and MMF for about 5 weeks after your transplant or until there are no signs of GVHD.

After your transplant, you will also get drugs to help speed up the recovery of white blood cells.

- We'll give you **Filgrastim** (G-CSF) through your catheter or by injection under your skin 5 days after your transplant (Day +5). You'll get Filgrastim every day until your blood counts are at a safe level and then continue for three additional days before stopping.

See Table 1 below for a schedule of when you'll get these drugs**.**

Table 1: Schedule of Drugs

Drugs	**Days -9 to -7**	**Days -6 to -2**	**Days -6 & -5**	**Day -1**	**Day 0 (Transplant day)**	**Days +3 & +4**	**Days +5 to +180**	**Days +5 to +35**	**Days +5 to +7 or more**
Thymoglobulin (ATG)	X								
Fludarabine		X							
Cyclophosphamide			X						
Total body irradiation (TBI)				X					
Transplant day (infusion of bone marrow)					X				
Cyclophosphamide						X			

Tacrolimus or cyclosporine							X		
Mycophenolate mofetil (MMF)								X	
Filgrastim									X

Your Transplant:

On your transplant day (Day 0), the donor cells from your haploidentical family member will be given to you through your catheter just like a blood transfusion. The cells will travel to your bone marrow where they will start to make new, healthy blood cells.

Health Evaluations:

We will test (evaluate) your health during the study. These tests and how often they are scheduled are standard care for patients receiving an allogeneic transplant. They would be done even if you were not part of this study. You will be watched closely for any signs and symptoms of GVHD.

After Your Treatment

Health Evaluations after Transplant:

- Routine blood tests (cell counts and liver and kidney function) two or three times per week until Day 28, then weekly until Day 100, and then at Days 180 and 365.
- One of six protocol-required 5 mL (~1 teaspoon) blood samples from a vein in your arm on Day 7 (4 of the other protocol-required samples will be taken pre-transplant on the days you receive ATG and 1 will be taken on the day of your transplant).
- Blood tests to see how well your immune system is working at Day 100, 180, and 365.
- Blood tests to find the amount of donor cells in your body on Days 28, 56, 100, 180, and 365. This is called chimerism.
- Blood tests to find out if you have any infections weekly until Day 100.
- Physical exam to look for toxicities on Days 28, 56, 100, 180, and 365.
- Physical exam to look for GVHD weekly until Day 100 and then at Days 180 and 365.
- Health-Related Quality of Life Questionnaires: If you speak English and are 8 years of age or older or if you speak Spanish and are 19 years of age or older, you will be asked to complete a questionnaire about your quality of life before your transplant and then at Day 100, Day 180, and Day 365.

6. Risks and Discomforts

You will have side effects while on the study. Side effects can range from mild to very serious. The risks listed in this section might happen from transplant. These risks might happen if you have a transplant as part of this study or as standard care. Your doctor will give you drugs to help lower the side effects, such as feeling sick to your stomach (nausea). In some cases, side effects can be long lasting or may never go away. The chemotherapy drugs can cause leukemia years later, but this is rare. These "secondary cancers" are often very hard to treat and can cause death.

Risks and Toxicities Related to Transplant:

The following problems may happen because of your transplant. These risks may happen if a transplant was done as part of the study or not. The risks are:

Death due to infection or transplant complications: Patients undergoing transplant for severe aplastic anemia are at risk of fatal complications due to several complications listed below (infection, organ damage, graft versus host disease, etc.). Although approaches to haploidentical transplant included in this study may improve outcomes, in past studies, as many as 20-40% of patients have had fatal complications using this stem cell source.

Slow recovery of blood counts: The red blood cells, white blood cells, and platelets can be slow to recover after a bone marrow transplant. Until your blood counts recover, you will need blood and platelet transfusions and you will be at risk for bleeding and infections. You'll receive Filgrastim to speed the recovery of the white cells as much as possible.

Graft failure: The stem cells (the "graft") may fail to grow inside your body. Past experience suggests that there can be up to a 10 - 15% chance of graft failure. If graft failure occurs, you could have low blood counts for a long period of time. If your counts don't recover, you may need to receive a second transplant. Graft failure can be fatal.

Graft-Versus-Host Disease (GVHD): GVHD happens when the donor cells recognize your body as foreign and attack it. In most cases, GVHD can be successfully treated. Sometimes GVHD is severe or difficult to treat and may lead to death. You will be watched closely for this complication and given drugs to prevent and/or treat it.

Acute GVHD, which can happen 0 – 3 months after transplant, may produce skin rash, nausea, vomiting, diarrhea, abdominal pain, abnormalities of liver function, and an increased risk of infection. Chronic GVHD, which can happen 3 months or later after transplant, may produce skin rashes, hair loss, thickened dry skin, dry eyes, dry mouth, liver disease, weight loss, diarrhea, and an increased risk of infection. To confirm the diagnosis of acute or chronic GVHD, you may be asked to have a biopsy (a small sample of your tissue to look at under the microscope) of your skin, gut, or, rarely, your liver.

Damage to the vital organs in your body: The transplant could cause problems in any body organ such as the heart, lungs, liver, gut, kidneys, bladder, or brain. The kidneys and the liver are most likely to be damaged. Some patients will experience serious lung problems from infections or the

chemotherapy and radiation.

Serious infections: Full and complete recovery of your immune system may take many months. During this time, there is an increased risk of infections. You will be prescribed certain drugs to reduce the chance of those 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 successfully treated, some infections may result in death.

Recurrence of disease or a new blood cancer: Your severe aplastic anemia may come back even if the transplant is successful at first. In rare cases, a new blood cancer may develop from the donor cells. Cyclophosphamide can cause damage to blood cells, which may result in a blood cancer such as myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML). These blood cancers usually develop 2 - 10 years after treatment, or 6 years on average. The risk of developing a new blood cancer after allogeneic transplant is probably less than 2%. If cancer develops in your blood cells, you may require additional treatment with chemotherapy or another blood or marrow transplant.

Risk to the unborn: The treatments in this study <u>have not</u> been proven to be safe at any stage of pregnancy. Therefore, if you are pregnant or nursing, you are not eligible for this study. Women who can become pregnant must use effective birth control while receiving chemotherapy, TBI, and drugs to prevent GVHD, and for 1 year after transplant. Effective birth control is defined as the following:

1. Refraining from all acts of vaginal sex (abstinence)
2. Consistent use of birth control pills
3. Injectable birth control methods (Depo-Provera, Norplant)
4. Tubal sterilization or male partner who has undergone a vasectomy
5. Placement of an IUD (intrauterine device)
6. Use of a diaphragm with contraceptive jelly and/or condoms with contraceptive foam every time you have sex.

<u>Reproductive Risks:</u>

The drugs used in this research study may damage your reproductive organs, affect your ability to have children, or possibly cause birth defects if you take them while you are pregnant. It is important that a woman is not pregnant or breast-feeding and does not become pregnant during the course of the study. Women may also want to talk to their doctors about freezing eggs prior to transplant.

- <u>If you are a woman and can become pregnant</u>:

  You will need to take a pregnancy test before you start the study. You should discuss ways to prevent pregnancy while you are in the study. Women who have gone through puberty may find that their menstrual cycle becomes irregular or stops permanently. This

does not mean that you cannot become pregnant. You must still use an effective method of birth control during your transplant and continue until 1 year after transplant.

Additional Information about MMF:

- MMF could be damaging to an unborn baby if you are pregnant or become pregnant while receiving the drug.
- MMF can make birth control pills less effective and increase your chances of becoming pregnant while you are taking it.
- If you can become pregnant, you must use 2 effective forms of birth control for 4 weeks before starting MMF, during treatment, and for 6 weeks after stopping MMF.
- In this study, you will be assigned to receive MMF for about 5 weeks, so you should not become pregnant during that time. If you think you might become pregnant or could become pregnant during the upcoming 5 weeks, you should not join the study.

- If you are a man:

  Your body may not be able to produce sperm (become sterile). You should talk with your doctor about banking your sperm before having a transplant. You must still use an effective method of birth control during your transplant and continue until 1 year after transplant.

Please check with your doctor to understand more about these risks.

Unforeseen Risks:

New risks might appear at any time during the study. These risks might be different from what is listed in this Consent Form. We will promptly tell you about new information that may affect your decision to take part in the study. We may learn new things about these types of transplants that might make you want to stop being in the study. We will let you know if this happens and you can decide if you want to continue in the study.

Other Treatments or Medications:

Some medicines react with each other, and it is important that you tell the study doctor or staff about any other drugs, treatments, or medicines you are taking. This includes over-the-counter drugs, vitamins, and herbal treatments.

It is also important that you tell the study staff about any changes to these medications during your participation in the study.

For more information about risks and side effects, ask your study doctor.

Risks and Toxicities Related to Medications:

Likely	What it means: This type of side effect is expected to happen in more than 20% of patients. This means that 21 or more patients out of 100 might get this side effect.
Less Likely	What it means: This type of side effect is expected to happen in 20% of patients or fewer. This means that 20 patients or fewer out of 100 might get this side effect.
Rare, but Serious	What it means: This type of side effect does not happen often – in fewer than 2% of patients – but is serious when it happens. This means that 1 or 2 patients (or fewer) out of 100 might get this side effect.

Possible Side Effects of Study Drugs

The most common side effects of the treatments used in this study are listed below. There is also the risk of very uncommon or unknown side effects. All chemotherapy drugs in this study are commonly used in transplant.

Fludarabine (Fludara®) – Chemotherapy drug

Likely	Less Likely	Rare, but Serious
▪ Infection ▪ Anemia (low red blood cell count) ▪ Tiredness ▪ Nausea ▪ Vomiting ▪ Pneumonia ▪ Mouth sores ▪ Fever ▪ Swelling of hands and feet ▪ Weakened immune system ▪ Pain ▪ Low number of white blood cells ▪ Low number of platelets in the blood ▪ Electrolyte imbalances	▪ Diarrhea ▪ Numbness and tingling in hands and/or feet ▪ Changes in vision ▪ Skin rash ▪ Cough ▪ Changes in heartbeat ▪ Loss of appetite ▪ Chills ▪ Lung inflammation	▪ Agitation or nervousness ▪ Confusion ▪ Difficulty breathing ▪ Weakness ▪ Severe brain injury and death ▪ Bleeding due to decreased number of platelets ▪ Kidney damage that could require dialysis ▪ Coma ▪ New (secondary) cancers

Thymoglobulin® (rabbit ATG, antithymocyte globulin rabbit) - Helps engraft cells and prevent GVHD

Likely	Less Likely	Rare, but Serious
▪ Fever/chills ▪ Hives ▪ Nausea ▪ Headache ▪ Body swelling ▪ Skin rash, joint aches and pain ▪ Shivering ▪ Serum sickness ▪ Low white blood cell count	▪ Severe or life-threatening allergic reaction ▪ Lymphomas (i.e., cancers of the immune system)	▪ Anaphylaxis ▪ Acute kidney failure ▪ High potassium

Cyclophosphamide (Cytoxan®) - Chemotherapy drug, helps prevent GVHD

Likely	Less Likely	Rare, but Serious
▪ Decreased white blood cell count with increased risk of infection ▪ Temporary hair loss ▪ Nausea ▪ Vomiting ▪ Loss of appetite ▪ Sores in mouth or on lips ▪ Diarrhea ▪ Stopping of menstrual periods in women ▪ Decreased sperm production in men ▪ Decreased platelet count (mild) with increased risk of bleeding ▪ Blood in urine	▪ Low red blood cell count (anemia) ▪ Temporary tiredness ▪ Damage to the fetus if you become pregnant while taking drug	▪ Scarring of lung tissue, with cough and shortness of breath ▪ Severe heart muscle injury and death at very high doses ▪ New (secondary) cancers

Filgrastim (G-CSF; Neupogen®) – helps speed up recovery of white blood cells

Likely	Less Likely	Rare, but Serious
▪ Ache or pain inside of bones ▪ Increased levels of liver enzymes and uric acid in the blood ▪ Low number of platelets in the blood ▪ Headache ▪ Tiredness	▪ Local irritation (skin) at the injection site ▪ Nausea ▪ Bleeding ▪ Fever	▪ Allergic reaction ▪ Enlargement or rupture of the spleen ▪ Worsening of pre-existing rashes ▪ Temporary hair loss ▪ Inflammation of a blood vessel in the skin

Mycophenolate Mofetil (MMF: CellCept®) – helps prevent GVHD

Likely	Less Likely	Rare, but Serious
▪ Miscarriage ▪ Birth defects ▪ Diarrhea ▪ Damage to unborn baby ▪ Limited effectiveness of birth control ▪ Stomach pain ▪ Nausea ▪ Vomiting ▪ Headache ▪ Tremors ▪ Low white blood cell count with increased risk of infection ▪ Swelling of the hands, feet, ankles or lower legs	▪ Low red blood cell count (anemia) ▪ Rash ▪ Difficulty falling asleep or staying asleep ▪ Dizziness ▪ Uncontrollable hand shakes	▪ Difficulty breathing ▪ Unusual bruising ▪ Fast heartbeat ▪ Excessive tiredness ▪ Weakness ▪ Blood in stool ▪ Bloody vomit ▪ Change in vision ▪ New (secondary) cancers ▪ Progressive Multifocal Leukoencephalopathy (a disease that damages the white/gray parts of the brain)

Total Body Radiation (TBI) – helps to weaken your immune system and prevent rejection of transplanted stem cells

Likely	Less Likely	Rare, but Serious
▪ Fever ▪ Fatigue ▪ Hair loss ▪ Loss of appetite ▪ Mouth sores ▪ Nausea ▪ Diarrhea ▪ Stomach cramps ▪ Vomiting (throwing up) ▪ Painful swelling of the salivary glands under the ears for a few days ▪ Low red blood cell count (anemia) ▪ Infection ▪ Bleeding ▪ Cataracts ▪ Hormone problems (such as thyroid disease or diabetes) ▪ Mouth sores	▪ Skin pigmentation (reversible) ▪ Sterility (inability to have children) ▪ Slow growth	▪ Lung fibrosis ▪ New (secondary) cancers

Tacrolimus (FK506, Prograf®) – GVHD drug

Likely	Less Likely	Rare, but Serious
▪ High blood pressure ▪ High blood sugar ▪ Low red blood cell count (anemia) ▪ High or low potassium levels ▪ Low magnesium and calcium levels ▪ Loss of appetite ▪ Diarrhea ▪ Nausea ▪ Fever ▪ Headache	▪ Hair loss ▪ Vomiting ▪ Tingling sensation in the extremities ▪ Itching ▪ Rash ▪ Abdominal pain	▪ Confusion ▪ Painful joints ▪ Increased sensitivity to light ▪ Change in vision ▪ Insomnia (trouble sleeping) ▪ Infection ▪ Jaundice (skin yellowing) ▪ Kidney injury ▪ Seizures ▪ RPLS/PRES[1]

[1] Reversible posterior leukoencephalopathy syndrome (RPLS) also known as posterior reversible encephalopathy syndrome (PRES). In transplant patients, it can be caused by some of the drugs used to prevent or treat GVHD. It can often, but not always, be prevented by very careful control of blood pressure.

It is very important that you DO NOT eat grapefruit or drink grapefruit juice while taking Tacrolimus. Grapefruit has an ingredient called bergamottin, which can affect some of the treatment drugs used in this study. Common soft drinks that have bergamottin are *Fresca*, *Squirt*, and *Sunny Delight*.

7. Other Treatments

It's optional to join this study. If you choose not to take part, you may still receive treatment with alternative immune suppressing therapy, new agents, or an allogeneic transplant to treat your disease. The transplant treatment and evaluations you would receive could be very similar to what you would receive if you join this study.

Your study doctor will talk with you about your options. If you decide not to participate in this study, your medical care will not be affected in any way.

Your other choices may include:

- Treatment with a partially-matched related or unrelated donor or another alternative donor source
- Treatment with other drugs to suppress the immune system without a transplant
- Treatment with drugs aimed at temporarily boosting your blood counts or other new agents under investigation
- Treatment with blood transfusions only
- Comfort care

Every treatment option has benefits and risks. Talk with your doctor about your treatment choices before you decide if you will take part in this study.

8. Possible Benefits

Taking part in this study may or may not make your health better. The information from this study will help doctors learn more about transplants for SAA. It could also help people with SAA that may need a transplant in the future.

9. New Information Available During the Study

During this research study, the study doctors may learn about new information about the study drugs or the risks and benefits of the study. If this happens, they will tell you about the new information. The new information may mean that you can no longer participate in the study, or that you may not want to continue in the study.

If this happens, the study doctor will stop your participation in the study and will offer you all available care to meet your needs and medical conditions.

10. Privacy, Confidentiality and Use of Information

Your confidentiality is one of our main concerns. Study records that have your name will be kept private as required by law. You will not be identified by name in the central study records. Your records will be given a unique code number. The key to the code will be kept in a locked file in the Principal Investigator's office.

All necessary steps will be taken to avoid you being identified in any public presentations. The results of this study treatment may be published in scientific journals in the future, but no patients (including you) will be identified.

Information about your transplant course may be reviewed or transmitted to national and international transplant registries, including:

- [Institution]
- The National Institutes of Health (NIH), which include the National Heart, Lung, and Blood Institute (NHLBI) and the National Cancer Institute (NCI)
- U.S. government agencies that are responsible for overseeing research such as The Food and Drug Administration (FDA) and the Office of Human Research Protection (OHRP)
- U.S. government agencies that are responsible for overseeing public health concerns such as the Centers for Disease Control (CDC) and federal, state, and local health departments
- The Data and Safety Monitoring Board (DSMB), not part of [Institution]
- Institutional Review Boards (IRBs) responsible for this study
- Blood and Marrow Transplant Clinical Trials Network Data and Coordinating Center (BMT CTN DCC), including:
    - The Center for International Blood and Marrow Transplant Research (CIBMTR)
    - The National Marrow Donor Program (NMDP)
    - Emmes, who are coordinating the studies of the BMT CTN
- Study investigators:
    - Dr. Amy DeZern, Co-Principal Investigator
    - Dr. Michael Pulsipher, Co-Principal Investigator

We will not identify you by name in any publications or reports that come from these organizations or groups.

Information that does not include personally identifiable information about this clinical trial has been or will be submitted, at the appropriate and required time, to the government-operated clinical trial registry data bank, which contains registration, results, and other information about registered studies.

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.

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Data regarding your clinical situation, including follow-up after 1 year, may be obtained from the CIBMTR, which captures information on all U.S. transplants.

For questions about access to your medical records, please contact:

[Insert name and phone number].

Expiration date for retention of records:

Information about the study results will stay in your research file at [insert institution] for at least 6 years or until after the study is completed, whichever is longer. At that time, either the research information not already in your medical record will be destroyed or your name and other identifying information will be removed from such study results. Research information in your medical record will be kept indefinitely.

11. Ending Your Participation

Being in this study is voluntary. You can choose to not be in this study or to leave this study at any time. If you choose not to take part in or leave this study, your regular medical care will not be affected in any way. Tell your doctor in writing if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing will be most helpful to you.

The study doctor or the study sponsor may stop the study at any time and we may ask you to leave the study. We may ask you to leave the study if you do not follow directions or if you suffer from side effects of the treatment. If we ask you to leave the study, the reasons will be discussed with you. Possible reasons to end your participation in this study include:

- You do not meet the study requirements.
- You need a medical treatment not allowed in this study.
- The study doctor decides that it would be harmful to you to stay in the study.

- You are having serious side effects.
- You become pregnant.
- You cannot keep appointments or take study drugs as directed.
- The study is stopped for any reason.

If you decide to leave this study after taking the study treatment or are asked to leave by your doctor for medical reasons, you'll need to come back to the doctor's office for tests for your safety. Even if you leave the study, the information collected from your participation will be included in the study evaluation.

12. Physical Injury as a Result of Participation

It is important that you tell your doctor, [investigator's name(s)], or study staff if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at [telephone number].

You will get medical treatment if you're injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

In case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

13. Compensation or Payment

You will not be paid for your participation in this research study. You will not be compensated or reimbursed for any extra costs (travel, meals, etc.) from taking part in this study.

14. Costs and Reimbursements

Most of the visits for this research study are standard medical care for your allogeneic transplant and will be billed to your insurance company. You and/or your health plan/insurance company will need to pay for some or all of the costs of standard treatment in this study.

You or your insurance will not be charged for tests that are only done for research on this study.

Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out if they will pay.

For questions about your costs, financial responsibilities, and/or medical insurance coverage for your transplant and this study, please contact /Center/Financial Counselor at /Number/.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

15. Ethical Review

The ethical aspects of this research study have been reviewed and approved by [name of IRB].

16. For More Information

If you need more information about this study, or if you have problems while taking part in this study, you can contact the study doctor or his/her staff. They can be reached at the telephone numbers listed here:

[Insert names and contact details]

17. Contact Someone about Your Rights

If you wish to speak to someone not directly involved in this study, or if you have any complaints about any aspect of the study, the way it is being conducted, or any questions about your rights as a research participant, you may contact:

[Insert appropriate contact details]

For questions about your rights while taking part in this study, call the [name of center] Institutional Review Board (a group of people who review the research to protect your rights) at [telephone number].

18. OPTIONAL Blood Samples for Trial-Related and Future Research Studies

This section of the Consent Form is about collection of optional blood samples for trial-specific and future research studies from people who are taking part in the study.

You can choose to give blood samples for optional trial-specific and future research studies if you want to. You can still be a part of the main study even if you say "no" to giving optional blood samples for these studies. Please mark your choice at the end of this section.

Researchers are trying to learn more about how the human body processes the drugs used for transplant and how the body recovers after transplant. This research is meant to gain knowledge that may help people in the future and make transplants even more successful.

If you agree to provide optional blood samples, here is what will happen:

- We'll take 24 mL (about 5 teaspoons) from your catheter or by a vein in your arm if you are an adult, or 12 mL (about 2.5 teaspoons) if you're a child (< 20kg). We'll collect this sample when you have your 1st check-up, before treatment starts.
    - This blood sample will be shipped on the day of collection to a qualified research laboratory that is partnering with the clinical trial team physicians for an important study related to this trial. This study wants to look at your telomeres, which are caps at the end of DNA strands to protect them. DNA is in your blood, so we can study telomeres using blood samples.
- At the same time, we will collect one additional 3 mL (about ⅔ teaspoon) blood sample.
    - This blood sample will be sent to the BMT CTN Biorepository for processing and storage for future genomic research studies. A repository is a place that protects, stores, and sends out samples for approved research studies. All research samples will be given a bar code that cannot be linked to you by future researchers testing your samples. A link to this code does exist. The link is stored at the Data and Coordinating Center for the Blood and Marrow Transplant Clinical Trials Network (BMT CTN DCC). The staff at the Repository where your sample is being stored does not have a link to this code. Your research samples will continue to be stored at the BMT CTN Repository until they are used up for approved research.
    - These samples will be kept and may be used in research to learn more about immune recovery, GVHD, severe aplastic anemia, cancer, and other diseases. When the samples are given to investigators for research, no information about your name, address, phone number, or other information that will let the researchers know who you are will be provided.
    - DNA from your stored blood samples and your health information might be used in genome-wide association (GWA) studies for a future project either done or supported

by the National Institutes of Health (NIH). Genome-wide association studies are a way for scientists to find genes that have a role in human disease or treatment. Each study can look at hundreds of thousands of genetic changes at the same time.

- If your coded samples are used in such a study, the researchers are required to add your test results and sample information into a public research database. This public database is called the NIH Genotype and Phenotype Database and it is managed by the National Center for Biotechnology Information (NCBI). The NCBI will never have any information that would identify you, or link you to your information or research samples. However, the results of genetic studies could, in theory, include identifying information about you.

  Your name and other information that could directly identify you (such as address or social security number) will not be placed into any scientific database. However, because your genetic information is unique to you, there is a small chance that someone could trace it back to you. The risk of this happening is small, but may grow in the future. Researchers have a duty to protect your privacy and to keep your information confidential.

Benefits

The research that may be done with your blood samples is not designed specifically to help you. The benefits of research using blood samples include learning more about what causes GVHD, severe aplastic anemia, cancer, and other diseases, how to prevent them, and how to treat them.

Risks

There is a small risk of an infection or fainting from the blood draw.

A possible risk is the loss of confidentiality about your medical information. We will do our best to make sure that your personal information is kept private. The chance that this information will be given to someone else is very small.

Some general things to think about when letting us store your blood samples for research are:

- The choice to let us collect and/or store blood samples for future research is up to you. No matter what you decide to do, it will not affect your care.
- If you decide now that your blood samples can be collected and stored for research, you can change your mind at any time. Just contact your study doctor in writing and let him or her know that you do not want us to continue storing your blood samples. His/her mailing address is on the first page of this form. Then any unused blood samples that remain will no longer be stored for research. However, samples and information that have already been shared with researchers cannot be taken back or destroyed.
- In the future, people who do research on these blood samples may need to know more about your health. While the study doctor or others involved in running this study may give the

researchers reports about your health, they will not give them your name, address, phone number, or any other information that will let the researchers know who you are.

Sometimes blood is used for genetic research (about diseases that are passed on in families). Even if your blood is used for this kind of research, you will not be told of the results and the results will not be put in your health records.

- Your blood will be used only for research and will not be sold. The research done with your blood may help to develop new products in the future. You will not get paid for any samples or for any products that may be developed from current or future research.
- Reports about research done with your blood will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an effect on your care.

Genetic Information Nondiscrimination Act

A new federal law (2009) called the Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and employers of 15 or more persons to discriminate against you based on your genetic information. Health insurance companies and group health plans may not request your genetic information that we get from this research.

This means that they must not use your genetic information when making decisions about your insurance. Be aware that this new federal law will not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Making Your Choice

Please read each sentence below and think about your choice. After reading each sentence, please indicate your choice below. If you have any questions, please talk to your doctor or nurse, or call our research review board at [telephone number].

No matter what you decide to do, it will not affect your care.

You can change your mind at any time about allowing us to use your samples and health information for research. However, samples and information that have already been shared with researchers cannot be taken back or destroyed.

Statement of Consent for Optional Blood Samples for Trial-Related and Future Research Studies

The purpose of collecting, storing optional blood samples, the procedures involved, and the risks and benefits have been explained to me. I have asked all the questions I have at this time and I have been told whom to contact if I have more questions. I have been told that I will be given a signed copy of this consent form to keep. I understand that I do not have to allow the collection and storage of my blood samples for study-specific and future research studies. If I decide to not let you store research samples now or in the future, it will not affect my medical care in any way.

I voluntarily agree that optional blood samples may be collected and that my blood samples and related information can be stored indefinitely by the BMT CTN Biorepository for research to learn about, prevent, or treat GVHD, severe aplastic anemia, cancer, or other health problems. I also understand that my DNA and health information may or may not be used in genome-wide association studies.

Telomere Research Study

❑ I do agree to give blood samples for a telomere research study.

❑ I do not agree to give blood samples for a telomere research study.

Future Genomic Research Studies

❑ I do agree to give blood samples for future genomic research.

❑ I do not agree to give blood samples for future genomic research.

_____ _____

Signature Date

Health Insurance Portability and Accountability Act 1 (HIPAA)[11] authorization to use and disclose individual health information for research purposes:

A. **Purpose**:

As a research participant, I authorize the Principal Investigators and the researcher's staff to use and disclose my individual health information for the purpose of conducting the research study, *Optimizing Cord Blood and Haploidentical Aplastic Anemia Transplantation*.

B. **Individual Health Information to be Used or Disclosed**:

My individual health information that may be used or disclosed for this research includes:

- Demographic information (for example: date of birth, sex, weight).
- Medical history (for example: diagnosis, complications with prior treatment).
- Findings from physical exams.
- Laboratory test results obtained at the time of work up and after transplant (for example: blood tests, biopsy results).

C. **Parties Who May Disclose My Individual Health Information**:

The researcher and the researcher's staff may collect my individual health information from:

[*List hospitals, clinics or providers from which health care information can be requested*].

D. **Parties Who May Receive or Use My Individual Health Information**:

The individual health information disclosed by parties listed in Item C and information I disclose during the course of the research may be received and used by the following parties:

- Principal Investigators and the researcher's staff:
  - Dr. Amy DeZern, Co-Principal Investigator
  - Dr. Michael Pulsipher, Co-Principal Investigator
- Study Sponsors:
  - National Heart, Lung, and Blood Institute (NHLBI) and the National Cancer Institute (NCI), both of the National Institutes of Health (NIH);
  - Blood and Marrow Transplant Clinical Trials Network Data and Coordinating Center (BMT CTN DCC), including the National Marrow Donor Program (NMDP), the Center for International Blood and Marrow Transplant Research (CIBMTR), and Emmes;

[1] HIPAA is the Health Insurance Portability and Accountability Act of 1906, a federal law related to privacy of health information.

- U.S. government agencies that are responsible for overseeing research such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP);
- U.S. government agencies that are responsible for overseeing public health concerns such as the Centers for Disease Control (CDC) and federal, state, and local health departments.
- The Data and Safety Monitoring Board (DSMB), not part of [Institution]
- Institutional Review Boards (IRBs) responsible for this study

E. **Right to Refuse to Sign this Authorization**:

I do not have to sign this Authorization. If I decide not to sign this Authorization, I will not be allowed to participate in this study or receive any treatment related to research that is provided through the study.

My decision not to sign this authorization will not affect any other treatment, payment, or enrollment in health plans or eligibility for benefits.

F. **Right to Revoke**:

I can change my mind and withdraw this authorization at any time by sending a written notice to the Principal Investigator to inform the researcher of my decision.

If I withdraw this authorization, the researcher may only use and disclose the protected health information already collected for this research study. No further health information about me will be collected by or disclosed to the researcher for this study.

G. **Potential for Re-disclosure**:

My individual health information disclosed under this authorization may be subject to re-disclosure outside the research study and no longer protected.

Examples include potential disclosures for law enforcement purposes, mandated reporting for abuse or neglect, judicial proceedings, health oversight activities and public health measures.

H. **This authorization does not have an expiration date.**

TITLE: BMT CTN 1502: Optimizing Haploidentical Aplastic Anemia Transplantation

Principal Investigator:

Name: Phone:

Address 1: Fax:

Address 2: Email:

For patients under 18, consent must be provided by the Legally Authorized Representative and Patient Assent is required (see **Assent Section** on the next page).

- I have had the chance to ask questions and understand the answers I have been given. I understand that I may ask questions at any time during the study.
- I freely agree to be a participant in the study.
- I understand that I may not directly benefit from taking part in the study.
- I understand that, while information gained during the study may be published, I will not be identified and my personal results will stay confidential.
- I have had the chance to discuss my participation in this research study with a family member or friend.
- I understand that I can leave this study at any time, and doing so will not affect my current care or prevent me from receiving future treatment.
- I understand that I will be given a copy of this signed consent form.

_____ _____

Participant Name Date

_____ _____

Participant's Signature (if 14 years or older) Date

I certify that I have provided a verbal explanation of the details of the research study, including the procedures and risks. I believe the participant has understood the information provided.

Name of Counseling Physician/Staff	Date
Signature of Counseling Physician/Staff	Date
Name of Interpreter	Date
Signature of Interpreter	Date

Pediatric Patient Assent

Study Title: **Optimizing Haploidentical Aplastic Anemia Transplantation**

Protocol: **BMT CTN 1502**

- **Why am I here?**

We invite you to join this research study because you need a transplant to treat your severe aplastic anemia. We will replace your unhealthy blood cells with blood cells from one of your family members. The new cells will travel to your bones and start making healthy cells in your body.

For this study, we will ask you for information about your health (health information) and for extra blood samples.

- **Why are you doing this study?**

We're doing this study to learn how well patients with severe aplastic anemia do with transplants that use haploidentical bone marrow.

- **What will happen to me if I join the study?**

If you say you want to be in the study, we will:

- Before your transplant:
  - Give you drugs to help your body get ready for the transplant. The drugs might make you feel sick. Your doctor will watch your health closely.
  - We will collect extra blood (about 1 teaspoon) 4 times before your transplant and 1 time on the day of your transplant. We will use a small needle to collect the blood from a vein in your arm, unless you have a central line in which case the samples will be collected through that central line. We will try to collect the extra samples at the same time as you have other blood tests done.
- After your transplant:
  - We will collect extra blood (about 1 teaspoon) one week after your transplant.
  - We will also give you drugs to help your body adjust to the new cells. The drugs might make you feel sick. Your doctor will keep watching your health after your transplant.

You will be in the study for 1 year after your transplant. About 30 people will be in the study.

- **Will the blood draw hurt?**

When we collect your blood from a vein in your arm, it may feel like a pinch. It will hurt for a minute and the place where the needle went might be red and sore. You might get a little bruise from the needle, but it goes away in a few days.

- **What if I have questions?**

You can ask any questions that you have about the study. If you forget to ask a question and think of it later, you can call me:

[insert office number].

You can also ask your question the next time you see me.

You can call the study office at any time to ask questions about the study.

- **How will you use my health information and blood samples?**

Your health information and blood samples will be used for this study and for future research about transplant in patients with severe aplastic anemia.

- **How will you store my health information and blood samples**?

Your blood samples will be sent to a qualified research lab for an important study.

All research samples will be tied to a number. This number will not be linked to your name or other identifying information.

A. Will the study help me?

We don't know if this study will help you or not. It may help other people who need a transplant in the future.

B. Will I be paid to be in the study?

No, you will not be paid to be in the study. It will not cost you anything to be in the study.

C. Do I have to be in this study?

If you don't want to be in this study, you need to tell us and your parent or guardian.

Your doctor will not be angry or upset if you do not want to join. You will still need to have treatment for your disease.

You can say yes now and change your mind at any time.

Please talk this over with your parents before you decide if you want to be in the study. We will also ask your parents to give their permission for you to join this study.

TITLE: BMT CTN 1502: Optimizing Haploidentical Aplastic Anemia Transplantation

Writing your name on this page means that you agree to join this study and know what will happen to you.

- I've been told what I will be asked to do if I am in this study.
- I've been told that I don't have to be in this study. I may quit the study at any time, and no one will be mad at me.
- If I want to quit the study, all I have to do is tell the person in charge.
- I've had a chance to discuss the study and ask questions. My questions have been answered.
- I agree to be in the study and do what I am asked to do for as long as I am in the study.
- My parents and I will get a copy of this form after I sign it.

_____	_____	_____
Patient's Name (if less than 14 years)	Date	Age (years)
_____	_____	_____
Signature of Child	Date	Age (years)

I have explained the purposes, procedures, and risks involved in this research study in detail to:

_____

Print name(s) of Parents/Authorized Consenting Party

AND

_____

Print child's name

Who in my opinion: _____IS _____IS NOT capable of assenting to participate in this study.

_____ _____

Signature of Person Conducting Assent Date