Patient Informed Consent Template for the BMT CTN 2207 Study

BMT CTN 2207

A Phase II Trial of Non-Myeloablative Conditioning and Transplantation of Haploidentical Related, Partially HLA-Mismatched, or Matched Unrelated Bone Marrow for Newly Diagnosed Patients with Severe Aplastic Anemia

Your Name: _____

Principal Investigator: *Insert local PI information*

Sponsor: This study is sponsored by the National Institutes of Health, through the Blood and Marrow Transplant Clinical Trials Network.

The ethics of this study have been reviewed and approved by the NMDP Institutional Review Board.

Sanofi US Services, Inc. has funded this study but did not write nor edit the protocol for scientific or medical detail. They will have no role in data analysis nor final publication content, other than acknowledgment of trial support.

Your study doctor or nurse will review this **Consent Form** with you, including:

- ✓ The purpose of the research
- ✓ Possible risks and benefits
- ✓ Other options available to you
- ✓ Your rights if you join the study

1. Study Overview

We invite you or your child ("you") to join this clinical trial, also known as a research study. We're doing this study to see how well transplant works for people with untreated severe aplastic anemia (SAA). We plan to enroll 60 patients who are between the ages of 3 years old and 75 years old on this study.

You're being asked to join because:

- You have a diagnosis of SAA, and
- Your SAA can be treated with an allogeneic transplant. An allogeneic transplant uses healthy blood forming cells donated by someone else to replace the unhealthy ones you have.
- You do **not** have a related donor whose cells fully match yours.
- You have a donor who is a half-match (called haploidentical) or an unrelated donor (a donor who is not related to you, that is the donor is not part of your family) who fully or partially matches you.

If you join, you'll:

- Be in the study for 1 year after the transplant.
- Get interventions including:
    - Cyclophosphamide ,
    - Filgrastim (G-CSF) ,
    - Fludarabine ,
    - Low dose total body irradiation ,
    - Mycophenolate mofetil ,
    - Tacrolimus ,
    - Thymoglobulin ,
- Take surveys.

Some possible risks and benefits of joining the study include:

- Possible Risks: You may have side effects from the drugs. The potential side effects of the interventions (drugs and radiation) in this study will be discussed later in this consent. There are many potential risks of having a transplant, regardless of whether you choose to participate in this research study. Your medical team will discuss the transplant process and potential risks of having a transplant with you. Many potential risks of transplant are the same, whether you decide to participate in this study or decide to receive a different transplant approach. Your medical team will explain these to you during the consent process for transplant.
- Possible Benefits: The transplant may cure your SAA but you may or may not benefit from being in this study. Knowledge we gain from this study may benefit others and may help doctors learn more about transplants for SAA.

If you do **not** join the study, you have other treatment options, such as:

- Treatment with other drugs to hold back the immune system and control your SAA without a transplant.
- Treatment with drugs that boost your blood counts for a short time.
- Treatment with other new drugs being studied.
- Treatment with blood transfusions with or without other medications.
- Treatment with a transplant outside of the study.
- Comfort care.

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.

Key points:

- Being in any research study is your choice.
- You may or may not benefit from being in the study. Knowledge gained from this study may help others.
- If you join the study, you can quit at any time. If you decide to quit the study, it will not affect your care at [name of facility or institution].
- Ask the study staff questions about anything you do not understand, or if you would like more information. You can ask questions now or at any time.
- 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.
- Take time to talk about the study with your doctor, study staff, and your family and friends. It is **your** choice to be in the study. No one can force you to join this study. If you decide to join, please sign the end of this Consent Form. You'll get a copy to keep.

2. Study Purpose

Severe Aplastic Anemia (SAA) is a life-threatening condition where the bone marrow does not make the normal amount of blood cells. Patients with aplastic anemia have low white blood cells (cells which fight infection), low red blood cells (cells that carry oxygen throughout the body), and low platelets (cells that help form clots and prevent bleeding). Treatments for SAA seeks to repair this abnormal immune system attack and allow the bone marrow to make the normal amount of blood cells. This can be done with a bone marrow transplant or sometimes with medications to suppress the immune system.

Historically, transplant therapy for SAA has been reserved for patients under 40 years old who had an available fully matched related donor. The standard treatment for older patients with SAA and patients who do not have a fully matched related donor has been treatment using transfusions, medications that suppress the immune system (immunosuppressive therapy, or "IST"), and medications that try to stimulate the bone marrow to produce more cells. For these older patients, transplant was used only if a patient did not respond to these treatments. However, progress has made transplants safer and allowed for half-matched related donor or full or partially-matched unrelated donors to be used with success rates similar to fully matched related donors in many situations. **The goals of this study are to determine if patients with SAA who have**

not received previous treatment for SAA can be treated effectively with transplant as their first SAA therapy.

When deciding whether to be a part of this study, it is important to understand the possible risks and benefits of other types of treatment. Immunosuppressive therapy (IST) is the standard treatment approach for patients without a fully matched related donor and can be an effective treatment for SAA, improving blood counts in 7-8 out of every 10 patients. For the patients that do not respond, transplant may be needed as a second treatment. Compared to transplant, IST has fewer early side effects. However, improving blood counts can take up to 6 months, and some patients treated with IST develop infections, a response to blood products received, and organ complications. About 1 out of 3 patients that were treated with IST and responded at first will have their SAA become a problem again, and need another treatment like transplant for their blood counts. Also, about 15 in every 100 adults and 2-3 in every 100 children with SAA treated with IST treatments develop blood cancers as a longer term risk. At 10 years after IST, only about 25 in every 100 adult patients are alive and do not have problems with SAA. For children, more than 50 in every 100 (about one half) are alive without need for more SAA treatment at 10 years when treated with IST.

In comparison to IST, transplant carries more short term and different longer term risks. Some side effects that can occur with transplant do not happen with IST. These include graft versus host disease where the donor cells can cause damage to skin, liver, GI tract and other organs. The chemotherapy and radiation needed for the transplant may also cause organ damage and reduced fertility. Some patients treated with transplant may still require therapy for their blood counts after transplant, and sometimes additional infusions of stem cells or, rarely, a second transplant is necessary. However, in most patients, transplant rapidly restores blood counts, allows patients to discontinue medicines for SAA, and produces a long-lasting SAA cure.

While transplant can be curative, many patients were not able to receive a transplant because they did not have a fully matched related donor. However, recent studies showed that transplant using half-matched related donors and unrelated donors can be effective in patients with SAA, with more than 90% of patients alive without recurrence of SAA.

This study builds on this prior experience, using the same medications and interventions. This is a phase 2 study. Studies in this phase test how well a new treatment will work to treat a disease. A pilot study in a single center has already been done to test safety, but this study will also continue to look at safety.

3. Study Treatment and Tests

You will have exams and tests done as part of the routine care for a bone marrow transplant. Your doctor will tell you about any routine exams, tests, and procedures. They'll also answer your questions. If there are any tests below that you don't think you've had or are worried about, please let your doctor know before agreeing to join this study.

Before Your Transplant

You'll need to have several tests to see if you can be in the study and have a transplant. These tests would be done before bone marrow transplant (but not generally before IST), even if you decide not to join this study. The tests include:

- Medical history.
- Physical exam, including height and weight.
- Blood and urine tests, including test that look for infections.
- Heart function tests (electrocardiogram [ECG]).
- Lung (pulmonary) function tests. Children will also have a test to measure how much oxygen is in their blood.
- Bone marrow tests. These tests are called aspirates or biopsies. A sample of your marrow will be taken from your hip bone with a large needle.
- A pregnancy test if you are able to have children. If you are pregnant, you will not be able to join this study.

During and After the Transplant:

Even if you decide not to join this study, many of the same events and tests will still take place. Regardless of therapy chosen, SAA patients require close medical follow-up, frequent laboratory monitoring, transfusion support, and receive many of the same medications to suppress the immune system and prevent infections.

Here is the schedule of events if you decide to enroll on study:

You will receive a combination of chemotherapy (chemo) drugs before you get your donor cells. This is called the conditioning regimen. It also includes 1 dose of radiation. It takes a little over 1 week to get the conditioning regimen.

The conditioning regimen takes out your immune cells and makes space in your bone marrow for the new donor cells to grow (engraft). Every patient in this study gets the same conditioning regimen.

On your transplant day (Day 0), the donor cells will be given to you through as an IV (intravenous) infusion, just like a blood transfusion. The cells will travel to your bone marrow where they should start to make new, healthy blood cells after several weeks.

Your doctor may decide to give you other medicines throughout your treatment to help with any side effects.

You will also need several tests after transplant to see how your body is doing with the treatment. These tests are part of regular care for patients who have had a transplant.

- Medical history, physical exam, height, and weight once a week for 4 weeks after transplant, then at Day + 100, Day + 180 and Day + 365. During these exams the doctor will look for any side effects you may have.
- Assessment of graft versus host disease (GVHD) once a week until Day +100, then at Day +180, and Day +365. GVHD is a possible side effect after transplant.

- Blood tests, including:
  - Blood counts – At least 2 times a week from Day 0 until your doctor says that your donor cells are making enough new blood cells, then once a week until Day +100, then at Day +180 and Day +365.
  - Electrolytes and liver function – 2 times a week for 4 weeks and then once a week until Day +100, then at Day +180 and Day +365.
  - Medication levels – As needed to make sure that the medication levels in your blood are at the right level for treatment without causing side effects.
- Bone marrow tests on Day +100, if your institution usually does them around that time, to see how your donor cells are engrafting.
- Other organ function testing as needed to see how well your heart, kidneys, liver, and lungs are working after transplant.

Table 1. Treatment plan

Conditioning regimens are always used in patients who get a transplant but they vary in how intense they are. This conditioning regimen is non-myeloablative or reduced intensity which means that the doses are not as high or toxic as many regimens used for transplants. The treatment plan is noted below. Medications to help prevent side effects will be given along with this study treatment. All days noted below are relative to your transplant day (Day 0).

Day	Treatment
-9, -8, -7	Thymoglobulin given 1 time each day as an intravenous (IV) infusion
-6, -5	Fludarabine and Cyclophosphamide given 1 time each day as an IV infusion
-4, -3, -2	Fludarabine given 1 time each day as an IV infusion
-1	Total body irradiation (TBI) 400 cGy dose
0	Transplant day – Infusion of donated cells
+3, +4	Cyclophosphamide and Mesna given 1 time each day as an IV infusion
+5	Begin taking: • Tacrolimus, given either as an IV infusion or a pill you swallow • Mycophenolate mofetil (MMF), a pill you take 3 times a day. • Begin filgrastim given as a shot under the skin each day until blood counts show signs that the donor cells are working.
+35	Stop taking MMF
+180	May start process to decrease or stop tacrolimus, if your doctor thinks it is time

Study-specific assessments/tests:

We will also ask you to fill out Patient Reported Outcome (PRO) surveys. These provide information on different aspects of your life before and after treatment. The surveys capture how you are feeling about your health and other impacts of treatment on your life. They are important for researchers to understand how this treatment affects patients in their everyday life. These surveys are **not part of usual transplant care and are for research only**.

You will take the surveys if you are:

- A study participant and 8 years old or older, **or**
- A guardian of a study participant who is 5-7 years old, **and**
- You can read and speak in English or Spanish.

The Survey Research Group (SRG) team from the Center for International Blood and Marrow Transplant Research (CIBMTR) will contact you to give you the surveys after the transplant. The SRG is part of the study team working with your study doctor.

You will be asked to complete surveys 4 times while you are in the study. Each survey will take 8 to 20 minutes to complete. You will take the surveys at these times:

- Before transplant.
- About 3 months after transplant.
- About 6 months after transplant.
- About 1 year after transplant.

You can skip any questions you do not want to answer.

You can also choose how to take the surveys:

- **Online:** SRG will send you a link to the survey. The link will not have any information that could identify you.
- **On paper**: SRG will send you the survey in the mail, with a stamped and addressed envelope to return the survey.
- **By phone:** SRG will call you and ask each survey question over the phone.

If we send you a survey but don't receive it back, the SRG may contact you by phone, email, or mail to make sure you got the survey and remind you to complete it. You can tell us how you would like to be contacted, and we will document your preference in a study form within our secure database.

The SRG's contact information is listed below. They will always contact you from these addresses or phone numbers. Team members will always say they are contacting you about this study and are from the Survey Research Group with CIBMTR.

Phone: 1-888-298-6714

Email: CureAA-Surveys@nmdp.org

Mailing Address: 500 N 5th Street, Minneapolis, MN, 55401-1206

We will share your contact information with the SRG so they can reach you for study surveys. If your contact information changes (for example, emails to you cannot be delivered), they may ask your study doctor or search online for updated contact information. They might need to use an internet-based search service to find you. By choosing to participate in this study, you are giving the SRG permission to search public and non-public information to try to find you.

Your survey answers will only be used for this study and will not be shared with your study doctor. We will not look at your answers to check for health issues. If you have any serious health issues or other concerns, immediately talk with your doctor or nurse.

For your time, you will be reimbursed $20 for each completed survey. You will be sent this payment within a month after SRG receives each completed survey.

Table 2. Timeline of Study Tests

Study Tests	Before treatment	Day 0	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42	Day 49	Day 56	Day 63	Day 70	Day 77	Day 84	Day 100	Day 180	Day 365
Blood samples for research (Optional)*	X					X				X					X	X	X
Routine blood tests	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Blood test for donor cell activity	X					X				X					X	X	X
Complete GVHD assessment			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Disease evaluation (bone marrow test)	X														X**	X**	X**
Heart function test (ECG)	X																
Infection assessment	X		X	X	X	X	X	X	X	X	X	X	X	X	X		X
Lung function test	X																
Medical history, physical exam, height and weight	X		X	X	X	X									X	X	X
Patient Reported Outcome surveys*	X														X	X	X
Pregnancy testing (if applicable)	X																
Toxicity assessment						X				X					X	X	X

*Exams and procedures done for research and would not be done with a routine transplant.
**Disease evaluation may be done at Day 100 and beyond if it's standard at your institution. Data may be provided to the study team for these, if printe available.

Stopping treatment

We'll stop the treatment if you:

- Tell your doctor you do not want to continue in the study.
    - ***Note: Study treatment can only be stopped before you get chemo and radiation. Once the you get the chemo to prepare your body for transplant, the study doctor would not be able to stop treatment, because it would be life-threatening.***
- Do not meet the study requirements.
- Need medical treatment not allowed in this study.
- Are having serious side effects.
- Become pregnant.
- Cannot keep appointments or take study drugs as directed.

We'll also stop the treatment if the study doctor decides that it would be harmful to you to stay in the study or 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.

Seeing your Research Results

Your doctor will share any results with you if they show that you need new treatment or need to change your treatment. If you'd like to see specific results, tell your doctor.

Timeline and Participants

You will be in the study for about 1 year. It will take about 4 years for researchers to complete the study. About 60 people will be in this study.

4. Risks and Benefits

Possible Benefits

Taking part in this study may or may not make your health better. If it works for you, you may need less treatment for your SAA. The information from this study will help doctors learn more about transplants for SAA. It could also help people with SAA who may need a transplant in the future.

Possible Risks

You may have side effects during the study. Side effects can range from mild to severe. Your health care team may give you medicine to help with certain side effects, like an upset stomach. In some cases, side effects can last a long time or may never go away. Side effects that are severe or do not get better with treatment can be life threatening. Patients can die from

complications of bone marrow transplant.

A common side effect of transplant with donor cells is graft versus host disease (GVHD). Sometimes, the donor's cells (the graft) begin to see your body (the host) as different. As a result, the donor cells may attack your organs and tissues, causing GVHD. It is a medical condition that can be very serious. Your treatment includes medicine to help prevent severe GVHD from happening. But it may happen anyway and you may need treatment. Alternatively, your cells can sometimes recognize the donor cells as different and not allow them to take hold and grow. This is called graft rejection or graft failure. It is a medical condition that can be very serious and requires additional treatment or a second transplant. Your treatment includes medicine to help prevent graft failure from happening. But it may happen anyway and you may need treatment.

Risks of Interventions

Table 3. What it means for a side effect to be "likely," "less likely," and "rare, but serious"

Likely	This side effect is expected to happen in **more than** 20% (20 out of 100) of patients.
Less Likely	This side effect is expected to happen in 20% (20 out of 100) of patients **or fewer**.
Rare, but Serious	This side effect does not happen often – in **fewer than** 2% (2 out of 100) of patients – but is serious when it happens.

Total Body Irradiation

Likely	Less Likely	Rare, but Serious
• Feeling tired • Fever • Infection, especially when white blood cell count is low • Low platelet counts, which may cause bruising or bleeding • Low red blood cell counts, which may cause tiredness or you may need blood transfusions • Mouth sores • Nausea, vomiting, stomach pain, diarrhea	• Eye cloudiness • Hair loss • Inability to have children • Painful swelling of the salivary glands under the ears for a few days • Redness of the skin	• Back pain • Children may have slower growth, which can affect how tall they are • Difficulty swallowing • Hormone problems • Kidney problems • Learning problems for children • Liver problems • Lung inflammation • Risk of developing other cancers in the future

Cyclophosphamide (Cytoxan) and Mesna

Likely	Less Likely	Rare, but Serious
• Blood in urine • Feeling tired • Hair loss, skin changes, rash, nail changes	• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath,	• A new cancer • Irregular heartbeat

Likely	Less Likely	Rare, but Serious
• Infection, especially when white blood cell count is low • Menstrual cycles (periods) may stop, so you might not be able to have children • Mouth sores, which may make it hard to swallow • Nausea, vomiting, diarrhea, loss of appetite, belly pain	swelling of the face or throat • Change in the levels of salts in the blood • Damage to the heart or heart failure, which may cause shortness of breath, swelling, cough or tiredness • Decrease in platelets which may cause bleeding • Decrease in red blood cells, which may require blood transfusions • Fluid around the heart • Loss of sperm so you might not be able to have children	• Kidney damage, which may cause swellingand you may need dialysis • Scarring of the lungs which may cause shortness of breath, fluid arounds the lungs • Swelling of the body including the brain, which may cause dizziness, confusion

Filgrastim (G-CSF)

Likely	Less Likely	Rare, but Serious
• Fever • Irritation at injection site • Low platelet levels, which may cause bruising or bleeding • Nausea	• Blood test results may not be normal, so you may need different IV medicines or more tests • Cough • Diarrhea • Dizziness • Feeling tired • General pain • Hair loss • Headache • High blood pressure • High levels of white blood cells • Infections • Inflammation of blood vessels in the skin • Large spleen • Low red blood cell counts, which may cause tiredness and you may need blood transfusions • Muscle spasms • Numbness • Pain in chest • Painful joints and muscles • Skin rash/redness • Trouble breathing	• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swollen face or throat • Low blood pressure • Lung damage with extra fluid in the lungs • Kidney damage • Ruptured spleen • Swelling

Fludarabine

Likely	Less Likely	Rare, but Serious
• Anemia (low red blood cells) which may require blood transfusions • Cough, shortness of breath • Feeling tired or irritable • Fever • Infection, especially when white blood cell count is low • Low platelet counts, which may cause bruising or bleeding • Nausea and vomiting, and loss of appetite • Pain	• Chills, increased sweating • Confusion • Damage to organs (brain, lungs, others) which may cause tiredness, changes in thinking or shortness of breath • Feeling of "pins and needles" in arms and legs • Hearing loss • Kidney damage, which may require dialysis • Mouth sores which may make it hard to swallow • Muscle pain • Rash • Swelling • Vision changes	• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swollen face or throat • Blood in urine • Coma, paralysis, seizures, stroke • Damage to liver, changing levels of liver enzymes in the blood

Mycophenolate Mofetil (MMF)

Likely	Less Likely	Rare, but Serious
• Blood test results may not be normal, so you may need different IV medicines or more tests • Difficulty breathing, cough, shortness of breath, fluid around the lungs • Headache • High blood pressure • Hormone birth control may not work • Low white blood cell count with increased risk of infection • Miscarriage, damage to unborn baby if pregnant while getting this medication • Nausea, vomiting, diarrhea, stomach pain • Swollen hands, feet, ankles, or legs • Skin rash • Tremors	• Change in the levels of salts in the blood • Decreased platelet count, which may cause blood loss in poop or vomit, more bruising • Difficulty falling asleep or staying asleep • Dizziness • Low blood pressure • Low red blood cell counts, which may cause tiredness and you may need blood transfusions • Joint or muscle pain	• Vision change • Fast heartbeat • A new cancer • Progressive Multifocal Leukoencephalopathy (a rare disorder caused by a virus that damages the brain), which can cause swelling or other problems • Severe difficulty breathing

Tacrolimus

Likely	Less Likely	Rare, but Serious
• Abnormal body movement, including tremors • Blood test results may not be normal, so you may need different IV medicines or more tests • Constipation, diarrhea, nausea, vomiting, reflux, lack of desire to eat • Difficulty sleeping • Dizziness • Feeling of "pins and needles" in arms and legs • Headache • High blood pressure which may cause dizziness or chest pain • Itching, rash • Kidney damage which may cause swelling and you may need dialysis • Liver damage • Low platelet levels, which may cause bruising or bleeding • Low red blood cell counts, which may cause tiredness and you may need blood transfusions • Low white blood cell counts, which may cause infections • Swelling of the body	• A new cancer • A tear or a hole in the bowels which may cause belly pain and you may need surgery • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swollen face or throat • Change in the heart rhythm, abnormal heartbeat, or heart stops beating • Damage to lungs, which may cause shortness of breath or fluid around lungs • Damage to brain, which may cause headache, seizure, blindness • Fluid around the heart • Heart attack or failure which may cause chest pain, swelling of ankles, and tiredness	• Damage to small blood vessels, which can cause small blood clots and possible organ damage.

Thymoglobulin ®

Likely	Less Likely	Rare, but Serious
• Fast heart rate • Fever • General pain, could also include joint and muscle pain • Headache • High blood pressure • High or low potassium levels in the blood • Infection, which may cause fever and chills • Low platelet levels, which may cause bruising, bleeding	• Blood test results may not be normal, so you may need different IV medicines or more tests • Feeling anxious • Rash, itching • Reaction to the medication infusion, which may include rash, fever, joint pain, muscle pain, and problems breathing • Sweating • Swelling • Problems sleeping	• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swollen face or throat • A new cancer

Likely	Less Likely	Rare, but Serious
• Low red blood cell counts, which may cause tiredness and you may need blood transfusions • Low white blood cells, which may cause infections and slower wound healing • Nausea, vomiting, diarrhea, constipation, stomach pain		

Other Treatments or Medicines

Some medicines react with each other, so it's important to tell the study doctor or staff about any other drugs, treatments, or medicines you're taking. This includes non-prescription or over-the-counter medicines, vitamins, and herbal treatments. It's also important that you tell the study staff about any changes to your medicines while you're in the study. For more information about risks and side effects, ask your study doctor.

Reproductive Risks

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 female is not pregnant or breast-feeding and does not become pregnant during the course of the study. Talk with your doctor before transplant about options that may be available to help preserve your ability to have children.

It is important that both women who can become pregnant and their male partners use effective birth control for at least 1 year after transplant while on this study or longer if they remain on medications that are harmful/potentially harmful to a fetus.

If you or your partner become pregnant during the study, the drugs used may hurt your baby. Doctors don't know all of the possible risks to your baby if you or your partner become pregnant during the study.

<u>If you are female:</u>
If you can become pregnant, 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. Nonetheless, you could still become pregnant. You must still use an effective method of birth control during your transplant and continue until you are finished with your transplant treatment. You may want to talk with your doctor about the possibility of collecting and storing your eggs until you are ready to have a child.

Effective birth control is defined as the following:

1. Not have any vaginal sex (abstinence)
2. Consistently use birth control pills or patch
3. Use an injectable birth control (for example, Depo-Provera or Norplant)

4. Have a tubal sterilization (tied tubes)
5. Have placement of an IUD (intrauterine device)
6. Use a diaphragm with contraceptive jelly every time you have vaginal sex

Or your partner must:

1. Have a vasectomy
2. Use condoms with contraceptive foam every time you have vaginal sex

Tell your doctor right away if you become pregnant during the study. Your doctor will discuss the risks to your unborn child and options with you.

If you are male:

Your body may not be able to produce sperm (become sterile). You should talk with your doctor before having a transplant about potentially storing your sperm until you are ready to have a child. Please check with your doctor to understand more about these risks. You must still use birth control during your transplant and continue for 1 year after transplant.

You must use one of the following birth control methods:

1. Not have any vaginal sex (abstinence)
2. Have a vasectomy
3. Use condoms with contraceptive foam every time you have vaginal sex.

Or your partner must:

1. Consistently use birth control pills or patch
2. Use an injectable birth control (for example, Depo-Provera or Norplant)
3. Have a tubal sterilization (tied tubes)
4. Have placement of an IUD (intrauterine device)
5. Use a diaphragm with contraceptive jelly every time you have vaginal sex.

Tell your doctor right away if your partner becomes pregnant during the study. Your doctor will discuss the risks to your unborn child and your options.

Surveys

There are very few risks with taking the study surveys. The main risk is that someone outside of the study team could see your answers. The study team will do everything it can to keep your answers confidential.

Also, some of the questions or topics may upset you. If this happens, your doctor can connect you with a counselor or trained support specialist, if needed.

Your doctor will not be able to see your answers on the surveys. The answers will not be shared with anyone until after the study is done and you will not be able to be identified.

Unforeseen Risks

Other 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 be in the study. There may be some unknown or unanticipated side effects from this treatment. The study team will do everything they can to keep you safe and lower your risk of side effects.

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

5. Your Rights to Withdraw, Ask Questions, and Seek Other Treatment

Being in this study is your choice. You can choose **not** to be in this study or leave this study at any time. If you choose to not join or leave this study, it won't affect your regular medical care in any way. If at any time you are considering leaving the study, talk to your study doctor about your health and safety.

You have the right to ask questions about the study at any time. If you have questions about the study, please contact:

[Insert contact details for Principal Investigator or study team]

If you want to talk with someone not directly involved in the study, or have any complaints or questions about your rights as a research participant, you may contact:

NMDP Institutional Review Board Administrator at: 1 (800) 526-7809

You must tell [insert name of Principal Investigator] if you decide to leave the study.

If you choose not to join, other options are available. Your study doctor will talk with you about your options. If you decide not to join this study, your medical care will not be affected in any way. If you join this study, and you are considering participating in another clinical trial at the same time, discuss this with your study doctor.

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

6. New Information Available During the Study

During this study, the study doctors may learn new information about haploidentical or unrelated donor transplant or the risks and benefits of taking part in the study. If they learn new information, they'll tell you as soon as it's available.

The new information may mean that you can no longer participate in the study, or you may not want to continue. If this happens, the study doctor will stop your participation and offer you all available care to meet your health care needs.

7. Privacy, Confidentiality, and Use of Information

Your privacy is very important to us. The study doctors, study sponsor, and other groups with access to your study-related medical information will do everything they can to protect it. Your confidentiality is one of our main concerns. We will do our best to make sure that the personal information in your medical record is kept confidential (private). However, we cannot promise total privacy.

The study doctors can protect your records if there is a court case. However, some of your medical information may be shared if required by law. If this happens, the study doctors will do their best to make sure that any information that goes out to others will **not** identify you.

To make sure the study is running fairly, some government agencies or other groups may need to access part of your medical records. For this study, those groups include:

- Sanofi US Services, Inc.
- NMDP Institutional Review Board (IRB).
- 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).
- The Data and Safety Monitoring Board (DSMB), not part of [Institution].
- Blood and Marrow Transplant Clinical Trials Network Data Coordinating Center (BMT CTN DCC), including:
    - The Center for International Blood and Marrow Transplant Research (CIBMTR).
    - NMDP.
    - The Emmes Company, who are coordinating the studies of the BMT CTN.

If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Study information may also be used for research in the future. These projects could be related to your disease or similar diseases, or development of approaches to treatment of this disease.

Private information, blood, or tissue taken during the study may be used for future research. The information, blood, or tissue will not be attached to you or your name in any way and the results of the research will not be given to you. To learn more, read Section 8 on Blood Samples for Future Research.

A description of this clinical trial will be available on ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

You will **not** be able to access your study results before the study is done. This helps keep the study results accurate and trustworthy.

When the study is complete, you can ask your study doctor for your health information from the study. **By signing this Consent Form, you agree to ask for your results only after the study is done.** You will still have access to your regular medical records.

The BMT CTN may get data about your health from the CIBMTR, including follow-up after 1 year. The CIBMTR captures information on all US transplants.

The expiration date for retention of records:
Information about the study results will stay in your research file at [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 stay there.

8. Leaving the Study

You can choose to leave the study at any time.

You may also be told to leave the study for reasons such as:

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

Even if you leave the study, the information already collected from you will be in the study evaluation. If you don't want your information included, you **must** let your study doctor know.

9. Cost and Reimbursement

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

Some health insurance plans will not pay for the costs of care when you take part in a research study. Check with your health insurance company to find out if they will pay.

You or your health insurance company will not be charged for extra tests or research costs associated with being in this study. Additionally, one of the drugs used in the conditioning regimen (Thymoglobulin) is being provided free of charge by the company that makes the drug.

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

You will **not** be paid for joining this study. You will not be paid or reimbursed for any extra expenses (such as travel or meals) from your participation in this study.

You will receive a $20 visa gift card when you complete the survey at each of the 4 visits (a total of up to $80 if you complete all surveys). This survey compensation may be taxable.

Physical Injury as a Result of Participation

Tell your study doctor or study team if you think you've been hurt because of being in this study.

You'll get medical treatment if you're hurt as a result of this study. Sanofi is not going to provide compensation unless the injury is a result of a defect in manufacture or formulation of the Study Drug or any Sanofi labeling or shipping errors of the study drug to the central pharmacy and only if the injury is not attributable to actions by the Blood and Marrow Transplant Clinical Trials Network Data Coordinating Center. You and/or your health insurance company will be charged for treatment unrelated to the study drug.

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

Statement of Consent for the Study

TITLE: BMT CTN 2207: A Phase II Trial of Non-Myeloablative Conditioning and Transplantation of Haploidentical Related, Partially HLA-Mismatched, or Matched Unrelated Bone Marrow for Newly Diagnosed Patients with Severe Aplastic Anemia

- I have read and understood this Consent Form. The purpose and description of the research study has been explained to me.
- 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 have had the chance to discuss my participation in this research study with a family member or friend if I choose.
- I understand that…
    - I may not directly benefit from taking part in the study.
    - My name and personal information will not be identified even if information gained during the study is published.
    - 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 will be given a copy of this signed consent form.
    - I do not give up any legal rights by signing this form.
    - I do not have to sign this consent form.
    - If I decide not to sign this consent form, I will not be allowed to participate in this study or receive any treatment related to research that is provided through the study.
    - I can change my mind and leave the study at any time by sending a written notice to the Principal Investigator.

_____
Printed Participant Name (or Parent/Guardian)

_____
Printed Legally Authorized Representative Name (if applicable)

_____ _____
Participant Signature (or Parent/Guardian or Legally Authorized Representative) Date (MM/DD/YYYY)

Physician Certification

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.

Counseling Physician Name

Counseling Physician Signature

Date (MM/DD/YYYY)

Interpreter Certification (if needed)

I certify that I have provided an accurate interpretation of this consent form. I believe the participant has understood the information provided.

Interpreter Name

Interpreter Signature

Date (MM/DD/YYYY)

10. Optional Blood Samples for Future Research

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

You can choose to give blood samples for 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 SAA. This research is meant to gain knowledge that may help people in the future and make treatment even more successful.

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

- We'll collect 38 mL (about 2 ½ tablespoons) of blood samples at 6 time points: before conditioning for transplant, and at 28 days, 56 days, 100 days, 180 days, and 365 days post-transplant.
    - Your blood samples will not be attached to you or your name in any way. Results of the research done with the samples will **not** be given to you.
    - The blood samples will be sent to the BMT CTN designated Biorepository for processing and initial storage.
    - Your blood samples may be stored in a repository designated by the BMT CTN and may be used for approved research studies by investigators in the broader scientific community. A repository is a place that protects, stores, and sends out samples for approved research studies.
    - Your name will be removed from the research sample and given a bar code. This bar code helps link your sample to de-identified data and other samples collected on this study by the Data and Coordinating Center for the Blood and Marrow Transplant Clinical Trials Network (BMT CTN DCC). Only the research team at your hospital will be able to link you to the research sample.
    - These samples may be used in research to learn more about immune recovery, GVHD, SAA, cancer, and other diseases. Researchers will not receive information about your name, address, phone number, or other information that will let the researchers identify you.
    - Samples will be stored until they are used up or until it is determined that they are not likely to be used in future research.

Genome-Wide Association (GWA) Studies

- DNA from your stored blood samples and your health information might be used in GWA studies for a future project either done or supported by the National Institutes of Health. GWA studies are a way for scientists to identify genes involved in human disease. This method searches the genome for small genetic changes that are more common in people with a particular disease than in people without the disease. Each study can look at hundreds of thousands of genetic changes at the same time.

Researchers use data from this type of study to find genes that may raise a person's risk of developing a certain disease

- If your genetic information is used in a GWA study, the researcher will add the DNA test results and non-identifying 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.

- 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 must protect your privacy and keep your information confidential.

- A federal law called the Genetic Information Nondiscrimination Act (GINA) 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 the genetic information that we get from this research. This means that they must not use your genetic information when making decisions regarding your health insurance. This federal law will not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

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, SAA, 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 them know that you do not want us to continue storing your blood samples. Their 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 affect your care.

Making Your Choice

Please read each sentence below and think about your choice. After reading each sentence, please mark 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.

If you withdraw consent for research use of your samples, there is no penalty or loss of benefits to which you are otherwise entitled. Data and samples that have not been shared will be withdrawn from any repository, if possible, but data already distributed for research use will not be retrieved.

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

The purpose of collecting and 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.

If I agree, I understand that optional blood samples may be collected and that my blood samples and related information can be stored indefinitely by the BMT CTN designated Biorepository for research to learn about, prevent, or treat GVHD, SAA, cancer, or other health problems. I also understand that my DNA and health information may or may not be used in GWA studies.

Future Research Studies

❑ Yes, I freely agree to give blood samples for future research.

❑ No, I do **not** agree to give blood samples for future research.

_____
Printed Legally Authorized Representative Name (if applicable)

_____ _____
Participant (or Legally Authorized Representative) Signature Date (MM/DD/YYYY)