Informed Consent to Participate in Research

Your Name: _____

Study Title: A Phase II/III Randomized, Multi-center Trial Comparing Sirolimus plus Prednisone and Sirolimus/Calcineurin Inhibitor plus Prednisone for the Treatment of Chronic Graft-versus-Host-Disease.

Protocol: 0801

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Sponsor: The National Institutes of Health (NIH) gave financial support for this research study through the Blood and Marrow Transplant Clinical Trials Network (BMT CTN).

Therakos, a company that manufactures the CELLEX^{TM} extracorporeal photopheresis device, has provided some financial support to help pay the costs of this study. This company did not plan or design this study. Therakos will not have a part in analyzing the results of this study.

Introduction
You are invited to join a research study. The primary goals of this study are to compare two treatments for chronic graft-versus-host disease (GVHD), and evaluate how well your chronic GVHD responds to treatment.

This study will be done over three years. One hundred people will participate at up to 50 clinics. Each clinic in this study will offer two study treatments. We will explain the two study treatments for your clinic in this Consent Form. Every clinic will report their results, so we can compare the two treatments at the end of the study.

The standard treatment for chronic GVHD is a corticosteroid (such as prednisone) and a calcineurin inhibitor (cyclosporine or tacrolimus). Patients who have chronic GVHD that is not controlled by the standard treatment usually have other drugs added to their treatment. Or less often, they may receive other drugs instead of standard treatment.

In this study chronic GVHD will be treated with another drug (sirolimus) in addition to either:

- A corticosteroid, or
- A corticosteroid and a calcineurin inhibitor, such as cyclosporine or tacrolimus

Sirolimus will be added to both treatments because research suggests that it may have positive effects on immune cells and improve GVHD treatment.

You will be randomly assigned to receive one of the two following treatments:

2-Drug Treatment	3-Drug Treatment
▪ A corticosteroid (such as prednisone) ▪ Sirolimus	▪ A corticosteroid ▪ A calcineurin inhibitor (cyclosporine or tacrolimus) ▪ Sirolimus

This study will try to learn if it is better to add sirolimus to standard treatment or to replace a calcineurin inhibitor with sirolimus.

This Consent Form will tell you about the purpose of the research, its possible risks and benefits, other options available to you, and your rights as a participant in the study. Please take your time to make your decision.

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.

1. Background

This research study is sponsored by The National Institutes of Health (NIH) through the Blood and Marrow Transplant Clinical Trials Network (BMT CTN). This study is being done to compare two treatments for chronic GVHD in people who have had an allogeneic transplant.

Chronic GVHD
Chronic GVHD is a medical condition that can become very serious. Chronic GVHD is a common development after allogeneic transplant. It happens when the donor cells attack and damage your tissues.

Chronic GVHD may cause:
- Skin rashes
- Mouth pain or dryness
- Eye dryness
- Nausea (feeling sick to your stomach) or diarrhea
- Liver inflammation
- Damage to other organs, such as the lungs, throat, and vagina

Treatments for chronic GVHD
Corticosteroid (or steroid) medications are the most basic treatment for chronic GVHD. However, less than half of patients will become free of chronic GVHD when steroid treatment is used alone. Several other drugs are often added to steroids to help treat chronic GVHD, including a calcineurin inhibitor (cyclosporine or tacrolimus) and/or sirolimus.

Information from earlier research suggests that different combinations of sirolimus, cyclosporine or tacrolimus, and steroids may help to reduce chronic GVHD.

Sirolimus, cyclosporine and tacrolimus all work by blocking the growth of new immune cells that can cause chronic GVHD. Research suggests that sirolimus also supports the growth of other immune cells called “T-regs” which limit the immune response that causes GVHD.

Cyclosporine and tacrolimus may slow the growth of these immune cells. Sirolimus, cyclosporine and tacrolimus are approved by the U.S. Food and Drug Administration (FDA) to prevent rejection after organ transplantation. They have been used for years as treatments for GVHD that do not respond to standard steroid therapy, or to prevent GVHD after allogeneic transplant.

2. Purpose

You are invited to join this research study because you have chronic GVHD that needs treatment.

The primary goals of this study are to compare two treatments for chronic GVHD and evaluate how well your chronic GVHD responds to your treatment. We will also collect extra blood samples for future research on GVHD.

3. Right 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 you want to leave the study, please contact:
[Insert contact info]

Being in this study is voluntary. You can choose to not be in this study, or leave this study at any time.

If you choose to not take part or to leave this study, your regular medical care will not be affected in any way. This includes standard care for your chronic GVHD. If you decide to leave this study after taking the study treatment, or are asked to leave by your doctor for medical reasons, you will be asked to come back to the doctor's office for tests for your safety.

Even if you withdraw from the study, the information collected from your participation will be included in the study evaluation, unless you specifically ask that it not be included.

Your study doctor and study staff will be available to answer any questions that you may have about your participation in, or your withdrawal from this study.

4. Procedures

Your study participation will last for 3 years, and includes your treatment and follow-up. One hundred patients will participate at up to 50 clinics around the country.

The number of required clinic visits during this time will depend on your treatment and the combination of drugs you receive. You will need to have health evaluations before you start treatment and for several years after you finish your treatment. These tests and examinations are

standard care for patients with chronic GVHD and would be done even if you were not part of this study.

One of the objectives of this study is to evaluate how the treatment affects the quality of the patient's life and whether there is a difference between the treatment arms. Therefore, all patients will be asked to complete questionnaires asking about their chronic GVHD symptoms and quality of life at study entry, 2, 6, 12, 24 and 36 months. It will take you approximately half an hour to complete the questionnaires.

If you decide to join, we will ask you to sign this Consent Form, and you will get a copy of the signed form to keep.

Before You Start Your Treatment
Before you join the study, we will evaluate your general health, medical history, and your current medications. It is important that you do not participate in the study if you suffer from an allergy to any of the drugs used in this study; or if you are pregnant, breastfeeding or are likely to become pregnant during the study.

You will have at least one clinic visit before you start your treatment for this study. This visit will collect information about your:

- Physical health (including history, height, weight and temperature)
- Comprehensive Chronic GVHD assessment [to include provider survey, patient survey, 2 minute walk (optional), grip test (optional) and Schirmer's eye exam (optional)]
- Lung function
- Cancer re-staging (if appropriate)
- Organs affected by GVHD
- Routine blood tests, including cell counts, cholesterol, liver and kidney function, and levels of GVHD treatment medications in your blood (if it applies to you)
- Blood samples (4-5 teaspoons, or 3-4 teaspoons for patients under 90 pounds) for protocol-defined GVHD studies
- Pregnancy test (if applicable)

Study Participation
You will receive either the 2-drug treatment or the 3-drug treatment.

If you are assigned to the 2-drug treatment, you will receive:

2-Drug Treatment
▪ Prednisone: once each day until 2 weeks improvement in GVHD symptoms is observed, and then slowly lowered and then stopped ▪ Sirolimus: once each day until all prednisone has stopped. After up to 3 months of stable improvement is observed, the amount of sirolimus will be slowly lowered and then stopped

If you are assigned to the 3-drug treatment, you will receive:

3-Drug Treatment
▪ Prednisone: once each day until 2 weeks improvement in GVHD symptoms is observed, and then slowly lowered and then stopped. ▪ Sirolimus: once each day. ▪ CNI: two times each day.

Depending on how well you respond to the treatment, you may need to visit the clinic every week for another 24 weeks. Your visits may drop to once each month, if your doctor feels it is appropriate. You may need to take your assigned treatment for up to two years. Your doctor will lower the amount of drugs you will need to take, as your chronic GVHD symptoms get better.

Once you stop taking your assigned treatment, the study team will follow your health for up to 2 years. Your total length of study participation may last up to 3 years, including follow-up once you finish your treatment.

Study Evaluations
We will evaluate your health at specific points during your study participation:

1. History, physical exam, and weight at 2, 3, 6, 12, 24 and 36 months.
2. Comprehensive Chronic GVHD assessment [to include provider survey, patient survey, 2 minute walk (optional), grip test (optional) and Schirmer's eye exam(optional)] to measure your response to treatment at 2, 6, 12, 24 and 36 months.
3. Routine blood tests, including: cell counts, and liver and kidney function, at least weekly for the first 4 weeks.
4. Cholesterol tests at 1, 2, 3, 6, and 12 months.
5. Lung (pulmonary) function tests at 3, 6 and 12 months.
6. Blood tests to check sirolimus levels will be done at least every week for the first 4 weeks and potentially twice a week if you are taking cyclosporine or tacrolimus.

Sirolimus levels from Week 5 to the end of your treatment are then done weekly to monthly, depending on your treatment.

7. Blood tests to check cyclosporine or tacrolimus levels are done at least weekly for the first 4 weeks and then at least monthly after Week 5 based on your treatment.
8. Blood samples (4-5 teaspoons, or 3-4 teaspoons for patients under 90 pounds) for protocol-defined GVHD studies at 2 months and 6 months or when any new oral or injected medication is added to treat your GVHD.

Randomization
A computer will randomly assign you to receive either the standard treatment or the study treatment. This means that you will be put into a group by chance. It is like flipping a coin or drawing names out of a hat. You will have an equal chance of being chosen for either treatment.

Additional Health Evaluations and Procedures
Before and after photographs may be taken to document your chronic GVHD.

5. Alternative Treatments

Current available treatments which may be used to treat graft-versus-host disease (GVHD) include:

- Corticosteroids (prednisone) with or without cyclosporine or tacrolimus (standard treatment for GVHD)
- Other medications
- Participation in another clinical trial (if available, check with your doctor)

Every treatment option has benefits and risks. Your study doctor will discuss these options with you. If you decide not to participate in this research study, your medical care will not be affected in any way.

6. Risks and Discomforts

It is very important that you do not eat grapefruit or drink grapefruit juice. 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*.

a.) Side Effects of Study Drugs and Treatments

All drugs can have side effects, including the standard therapy for GVHD (steroids) and the other drugs being tested in this study. Your doctor will watch you carefully and will change your treatment if side effects develop.

Please see Table: Risks and Side Effects of Study Drugs and Treatments at the end of this section for more information on the drugs used in the study treatments.

b.) Infections

Because chronic GVHD is caused by an immune attack on your tissues from the transplanted donor cells, all treatments for chronic GVHD include drugs to control (suppress) that immune attack. There is a higher risk of infection in patients with chronic GVHD and in people who take steroids like prednisone or methylprednisolone, the standard therapy for chronic GVHD.

You will need to take several antibiotics to prevent infection. You will also be watched carefully for any infections while you are being treated for chronic GVHD. Tell your doctors promptly if you get a fever, chills, cough or any other symptoms that might be a sign of an infection.

c.) Risks of Other Procedures Including Blood Draws

There are no major risks associated with drawing blood. Having your blood drawn can be uncomfortable and can sometimes cause a bruise. In rare cases, a blood draw can cause fainting. Only trained people will draw your blood.

d.) Reproductive Risks

The drugs used in this research study, including sirolimus and CNIs may cause injury or birth defects if you take them during pregnancy. Because of this, it is important that you are not pregnant or breast-feeding and do not become pregnant during the course of the study.

If you are a woman and pregnancy is a possibility, you will need to take a pregnancy test before you start the study. You should discuss ways to not become pregnant while you are participating on the study.

e.) Unforeseen Risks

New risks might appear at any time during the study that are different from the risks listed in this Consent Form. We will promptly tell you of any new information that may affect your decision to participate.

f.) 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 non-prescription medications, 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.

Table: Risks and Side Effects of Study Drugs and Treatments

	Prednisone	**Sirolimus**	**Calcineurin Inhibitor (Cyclosporine or Tacrolimus)**
Common (more than 20% of patients)	▪ Fluid retention and bloating ▪ Problems with the liver, pancreas or adrenal glands ▪ High blood pressure ▪ Enlarged heart ▪ Muscle wasting ▪ Thinning of bones ▪ Torn tendons ▪ Stomach ulcers ▪ Slow wound healing ▪ Thin fragile skin ▪ Broken blood vessels in the skin, esp. face ▪ Diabetes ▪ Slowed growth in children ▪ Cataracts ▪ Mood swings or emotional changes ▪ Insomnia	▪ High blood pressure ▪ Nausea (feeling sick to your stomach) ▪ Diarrhea and/or constipation ▪ Infection ▪ Fever ▪ Liver or kidney problems ▪ Weight gain ▪ Muscle pain ▪ High cholesterol ▪ Acne	▪ Headache and/or dizziness ▪ Uncontrollable shaking of a part of the body ▪ Diarrhea and/or constipation ▪ Nausea and/or vomiting ▪ Heartburn ▪ Stomach pain ▪ Loss of appetite ▪ Difficulty falling asleep and/or staying asleep ▪ Weakness ▪ Back and/or joint pain ▪ Burning, numbness, pain, or tingling in the hands or feet ▪ Rash ▪ Itching

Table: Risks and Side Effects of Study Drugs and Treatments, continued

	Prednisone	Sirolimus	Calcineurin Inhibitor (tacrolimus or cyclosporine)
Less Common (less than 20% of patients)		▪ Chest pain ▪ Insomnia (unable to sleep) ▪ Upset stomach or vomiting ▪ Shortness of breath ▪ Low blood counts ▪ Skin rashes or hives ▪ Slow wound healing	
Rare but Serious (less than 2-3% of patients)		▪ Low blood pressure ▪ Lung problems, including asthma ▪ Loss of appetite ▪ Serious infections ▪ Blood clots ▪ Skin problems ▪ Kidney failure ▪ Secondary cancers ▪ Bone degeneration (necrosis)	▪ Decreased urination ▪ Pain or burning on urination ▪ Swelling of the arms, hands, feet, ankles, or lower legs ▪ Weight gain ▪ Unusual bleeding or bruising ▪ Seizures ▪ Coma (loss of consciousness for a period of time)

7. Possible Benefits

Taking part in this study may or may not make your health better.

We do know that the information from this study will help doctors learn more about possible therapies for the treatment of chronic GVHD. This information could help future allogeneic transplant patients.

New Information Available During the Study
During this research study, new information about the study drug or the risks and benefits of the study may become known to the study doctors. 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 you will be offered all available care to suit your needs and medical condition.

8. Privacy, Confidentiality and Use of Information

Your confidentiality is one of our main concerns. We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy.

Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. Your study number is not related to your name, social security number or medical record number at [insert facility name].

Information about your transplant from your original medical records may be seen or sent to national and international transplant registries, including:

- The Center for International Blood and Marrow Transplant Research (CIBMTR)
- The National Marrow Donor Program (NMDP)
- The Food and Drug Administration (FDA)
- The National Institutes of Health (NIH), which include the National Heart, Lung, and Blood Institute (NHLBI) and the National Cancer Institute (NCI)
- Data and Coordinating Center of the Blood and Marrow Transplant Clinical Trials Network (BMT CTN)
- Other authorized study organizations

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

9. Ending Your Participation

The study doctor or the study sponsor may stop the study at any time. 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 you are asked 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.

10. Physical Injury as a Result of Participation

It is important that you tell your study doctor or study staff if you feel that you have been hurt or injured because of taking part in this study.

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. This 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.

11. Compensation or Payment

You will not be paid for your participation in the research study. You will not get compensation or reimbursement for any extra expenses (travel, meals, etc.) you may have through your participation on this trial.

12. Costs & Reimbursements

Most of the visits for this research study are standard medical care for patients with GVHD 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.

13. Ethical Review

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

14. Further Information

If you need any information about this study, or if you have any problems while you are participating in this study you can contact the study doctor or his/her staff. They may be contacted at the telephone numbers listed here.
[Insert name and contact details]

15. Independent Contact

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

16. Web Information

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.

Health Insurance Portability and Accountability Act 1 (HIPAA[1]) 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:

A Phase II/III Randomized, Multi-center Trial Comparing Sirolimus plus Prednisone and Sirolimus/Calcineurin Inhibitor plus Prednisone for the Treatment of Chronic Graft-versus-Host-Disease.

B. Individual Health Information to be Used or Disclosed

My individual health information that may be used or disclosed to do 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 treatment (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

[1] HIPAA is the Health Insurance Portability and Accountability Act of 1996, a federal law related to privacy of health information

The individual health information disclosed by parties listed in item c and information disclosed by me during the course of the research may be received and used by the following parties:

- Principal Investigator and the researcher's staff
  Paul Carpenter, M.B., B.S., Co-Investigator
  Mutka Arora, M.D., Co-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 (BMT CTN)
- 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.

E. Right to Refuse to Sign this Authorization

I do not have to sign this authorization. If I decide not to sign the 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 or abuse or neglect, judicial proceedings, health oversight activities and public health measures.

H. This authorization does not have an expiration date.

Blood and DNA Samples for Research

Please note: This section of the Informed Consent Form is about an additional research study that will be done with people who are taking part in the main study. You may take

part in this additional study if you want to. You can still be a part of the main study even if you say 'no' to take part in this additional study.

Your blood and cells have a material known as DNA. This is a molecule that holds a person's genetic information.

We ask for your permission to collect and store extra blood and DNA. These samples will be used for future research.

DNA from your stored blood and DNA 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 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 add to a person's risk of developing a certain disease.

If your coded genetic and clinical information is used in such a study, the researcher is required to 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.

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 regarding insurability. 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.

Procedures

- We will collect extra blood samples at the same time you have routine blood tests done on 3 study visits; before you start treatment (baseline), 2 months and 6 months.
- The amount of blood collected from you is small – about 2 teaspoons (10mL) each time.
- We will also collect samples of your DNA by swabbing four sections of the inside of your cheeks with cotton swabs.
- Your blood and DNA samples will be collected confidentially and your name will not be on the containers.
- These samples may be stored indefinitely for future research.

Withdrawal
If you agree to allow your blood and DNA samples to be used for research, you can change your mind at any time. If you change your mind, please contact [the Principal Investigator at your transplant center] in writing to state that you are withdrawing permission for your blood to be used for research. His/her mailing address is on the first page of this Consent Form. Any unused samples will be destroyed if you withdraw your permission. **If you choose not to participate in this additional research there will be no change in your care.**

Benefits
You will not benefit directly from providing blood and DNA samples for this study.

Risks
There are no major risks associated with drawing blood. Having your blood drawn can be uncomfortable and can sometimes cause a bruise. In rare cases, it can cause fainting. Only trained people will draw your blood. There are no major risks with swabbing the inside of your cheeks.

Confidentiality and Your Medical Information
The results of GVHD research done with your blood and DNA will not be part of your medical record and will not be shared with you.

If you agree to allow your blood and DNA samples to be used for research, they will be collected confidentially and your name will not be on the tubes. Only the study doctors or staff working with them will study the results from your blood and DNA samples.

Information gained from research on your blood and DNA may be used to develop diagnostic procedures or new treatments for GVHD in the future. Your blood will not be sold to any person, institution, or company for financial gain or profit.

Making Your Choice
Please read each sentence below and think about your choice. After reading each sentence, make your selection by checking one of the boxes. If you have any questions, please talk to your doctor or nurse, or call our research review board at [IRB's phone number].

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

❑ I agree to allow my blood and DNA to be used for future research.

❑ I do not agree to allow my blood and DNA to be used for future research.

Signature *Date*_____

TITLE: A Phase II/III Randomized, Multi-center Trial Comparing Sirolimus plus Prednisone and Sirolimus/Calcineurin Inhibitor plus Prednisone for the Treatment of Chronic Graft-versus-Host-Disease.

_____ _____
Participant Name Date

_____ _____
Participant Signature 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.

_____ _____
Counseling Physician Date

_____ _____
Signature of Counseling Physician Date

Assent to Participate in Research

Study Title: A Phase II/III Randomized, Multi-center Trial Comparing Sirolimus plus Prednisone and Sirolimus/Calcineurin Inhibitor plus Prednisone for the Treatment of Chronic Graft-versus-Host-Disease.

Protocol: 0801

A. Why am I here?

We are inviting you to join our study because you have chronic graft-versus-host disease (GVHD).

Chronic GVHD happens when donor cells from your transplant attack parts of the body like your skin, stomach or liver. Both children and adults can get chronic GVHD. It can be a very serious problem for some people.

B. Why are you doing this study?

We want to compare two ways to treat chronic GVHD. This will help us learn which may be a better treatment.

C. What will happen to me?

If you say you want to be in the study, we will ask you for several things:

- Permission to let us read your medical records and x-rays.
- Check-ups with the study doctors.
- Some blood from you (about 3-5 teaspoons). A very small needle will be used to get blood.
- Answer some questions about how you feel.

You will be assigned to have either Treatment #1 or Treatment #2. The doctors will use a computer to decide who goes into each group. Each treatment uses a different mix of drugs.

Treatment #1	**Treatment #2**
▪ A steroid	▪ A steroid
▪ Cyclosporine or tacrolimus	▪ Sirolimus
▪ Sirolimus	

We will watch you carefully for fevers, any sign of infection or other problems.

D. Will it hurt?

When you have your blood taken with a needle, it may feel like a pinch. It will hurt for a minute and sometimes the place where the needle went might be red and sore. You might get a little bruise where the blood was taken but it goes away in a few days.

E. Will the study help me?

We don't know if the study will help you or not. Your GVHD may stay the same, it may get better, or it may get worse.

F. 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.

G. Do I have to be in this study?

If you don't want to be in the study, you need to tell us and your parent or guardian. Your doctor will not be angry or upset if you don't want to join.

Whether you are in the study or not, you will still need to have treatment for your GVHD.

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

Please talk this over with your parent or guardian 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.

Use of Blood and DNA Samples

Some of your blood will be used to test for GVHD. Additional blood (1-2 teaspoons) and a sample of cells from inside your cheek (DNA) will be collected and saved for future studies. Your blood has a material known as DNA. DNA is a molecule that holds your genetic information. We may study your blood and your DNA in future GVHD research.

To be in the study, you must agree to have your blood used for GVHD and other regular tests, but you do not have to agree to have your blood or cheek cells (DNA) used in future research.

Please check one of the boxes below to show how you want your blood and cheek cells (DNA) to be used.

- ❒ Yes, you may use my blood and cheek cell (DNA) samples for future research.
- ❒ No, you may not use my blood and cheek cell (DNA) samples for future research.

Writing your name on this page means that you agree to be in the study, and know what will happen to you. If you decide to quit the study, all you have to do is tell the person in charge.

You and your parent or guardian will get a copy of this form after you sign it.

_____ _____
Signature of Participant's Guardian Date

_____
Printed Name of Participant's Guardian

_____ _____
Signature of Participant (if 18 years old or older) Date

_____
Printed Name of Participant

_____ _____
Signature of Researcher Date

_____
Printed Name of Researcher