Official Study Title: A PHASE II PEDIATRIC STUDY OF A GRAFT-VS.-HOST DISEASE (GVHD) PROPHYLAXIS REGIMEN WITH NO CALCINEURIN INHIBITORS AFTER DAY +60 POST FIRST ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT FOR HEMATOLOGICAL MALIGNANCIES

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A PHASE II PEDIATRIC STUDY OF A GRAFT-VS.-HOST DISEASE (GVHD) PROPHYLAXIS REGIMEN WITH NO CALCINEURIN INHIBITORS AFTER DAY +60 POST FIRST ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT FOR HEMATOLOGICAL MALIGNANCIES

Note: When we say "you" in this consent, we mean "you or your child." When we talk about research, it can be called a clinical trial, research study, or research protocol.

Key Information

To start, we want to highlight the risks and study requirements that we think you should know before deciding if you want to take part in this research study. If you're still interested, we'll then get into more detail.

A. Why are you being asked to volunteer in this study?
You are being asked to take part in this clinical trial because you have a lymphoid based cancer diagnosis that requires a bone marrow transplant.

B. What is the usual approach to this cancer?
When you get a transplant, the transplanted cells will see your body as different and will try to fight your body. The symptoms of this fight can be bad and make you very sick. As a group, the symptoms are called graft-versus-host disease (GVHD for short). The GVHD symptoms can happen just about anywhere in your body. They can happen right away or later. To decrease the chance of getting GVHD, doctors normally give patients a drug called cyclosporine A (CsA) until day +100 post-transplant and methotrexate (MTX). CsA is a calcineurin inhibitor (CNI) drug and works in a certain way.

C. Why is this study being done?
Instead of giving you CsA until day +100 post-transplant, your doctors would like to give it until day +60 post-transplant and substitute it with a new drug called ruxolitinib which will be added on day +40 post-transplant. This is because CsA has many side effects which increases risk for complications during transplant. Also, it affects the ability of the donor lymphocytes to kill leukemia cells. Ruxolitinib works in a different way than CsA and is well tolerated. It also does not affect the ability of the donor lymphocytes to kill leukemia cells. We will test the combination of CsA with MTX and ruxolitinib to see if the chance of getting any type of GVHD symptoms decreases. The new drug ruxolitinib is approved by the FDA for treatment of bad cases of GVHD.

D. What will happen if you decide to take part in this study?
To start, you will get the standard (normal) 9 or 10- day treatment before transplant:

- 4 days of radiation (x-rays) to your whole body, twice a day, then
- A drug called cyclophosphamide will be given in an IV once a day for 2 days.
- Another drug called mesna is given before and after the cyclophosphamide to decrease its side effects.
- A drug named rabbit ATG may be given if you have an unrelated donor for your transplant. If so, then you will get the rabbit ATG once a day for 3 days.

Then, you will get a bone marrow transplant by IV.

To keep the chance of GVHD low, you will get the normal drugs, CsA and MTX by IV. About 12 hours after each dose of MTX you will get another drug, leucovorin, that helps decrease the toxicity associated with MTX. MTX will be given on 4 different staggered days over 11 days. You will continue to receive the CsA for 60 days and then it will be stopped.

You will also take the new drug ruxolitinib starting day +40 post-transplant twice a day by mouth for at least 3 months to decrease the chance of getting GVHD symptoms. We will watch you closely and if you do get any symptoms, find out if they are not as bad as we would normally expect. We expect that you will take part in this study for one year after your transplant.

E. What are the research risks and benefits of taking part in this study?
Your risks are mainly related to the transplant and the preparation for it. You could have serious and possibly fatal disorders such as GVHD, stopped up blood vessels, way too many white blood cells, infection, bleeding, anemia, and major problems with your mucous membranes. As the normal drug CsA will be stopped early it may increase your risk of GVHD. The new drug ruxolitinib may cause anemia or a decrease in the white cell count. There may be no benefit to you. However, it's possible that you may not get as bad of a case of GVHD. Also, this study may help future transplant patients.

F. How many people will take part in this study?
About 30 people will enroll on this study.

G. What are your options?
   a. Taking part in this research study is completely your choice.
   b. If you decide to take part in this study, you can change your mind and stop at any time.
   c. If you decide not to take part in this study, you may still be able to receive care at St. Jude.
   d. You may choose to take part in another research study if available.
   e. You may choose no treatment or to seek treatment somewhere else.

If you are still interested in taking part in this research study, [CNI60], more detail will be provided in the following pages.

Table of Contents

1. Why are you being asked to volunteer for this research study?

You are being asked to take part in this research study because you have a lymphoid based cancer requiring a transplant. Please take your time in deciding and feel free to discuss it with your family, friends, and St. Jude's staff. Before you agree, it is important that you read this informed consent document that describes the study. After you understand the research study and if you agree to take part, you will be asked to sign this form. You will be given a copy to keep.

2. Who is sponsoring this study?

This study is being sponsored by St. Jude Children's Research Hospital. The study doctor is Dr. Ashok Srinivasan. He can be reached by telephone at 901-595-3300 if you have questions or concerns about this study.

Dr. Kim Nichols, an investigator of this study, has a financial relationship with Incyte, Inc., a publicly-traded pharmaceutical company providing drug for this study. Your enrollment in this trial and its outcome will not cause Dr. Nichols to receive a financial benefit from Incyte.

3. What is the purpose of this study?

The purpose of the study is to find out if it is safe to stop Cyclosporine A (CsA) early on day +60 rather than continuing until day +100 post-transplant, by substituting it with a new drug called ruxolitinib. We will determine if the new drug ruxolitinib given with cyclosporine and methotrexate is safe and effective in preventing GVHD after a transplant. We will follow your progress for a year after your transplant.

4. What will be done in this study?

You will be in the hospital at first. An IV line will be put in so that conditioning treatments can be given that way. Conditioning is the treatment that gets your body ready to accept the transplant. Your conditioning treatment will begin about 10 days before your transplant. The table below describes the treatment you will receive. The conditioning treatments below is standard of care and used in most transplants. You will also receive treatment to prevent GVHD with CsA and MTX which is standard of care and used in most transplants. In this clinical trial CsA is being discontinued early on day +60 and being substituted by ruxolitinib the new drug on day +40 post-transplant.

Schedule	Medication or Procedure Name
Days -7, -6, -5 and -4	Total Body Irradiation (radiation treatment)
Days -3 and -2	Cyclophosphamide (a chemotherapy)
Days -3 and -2	Mesna (a drug to prevent treatment side effects)
Days -3, -2 and -1	Rabbit ATG (an antibody, used only if your donor is not matched brother or sister)
Day -1	Cyclosporine treatment begins (a treatment to prevent GVHD)
Day 0	Bone marrow infusion
Days +1, +3, +6 and +11	Methotrexate (a treatment to prevent GVHD)
Day +40	*Ruxolitinib treatment begins (a treatment to prevent GVHD)

The minus sign (-) means before your transplant. Day 0 is the transplant day. The plus sign (+) means after your transplant.

** New drug being studied in this clinical trial*

During and after these treatments, we will keep watching you and checking in to see how you are feeling. We will do lots of tests the 28th day (about a month) after your transplant to see if it is progressing as expected.

When you are feeling well enough, you will be able to move out of the hospital and into St. Jude housing. You will keep taking cyclosporine daily for 60 days. After you start ruxolitinib on day +40 you will continue taking it twice a day for 100 days post-transplant. We will check you regularly during this time. After 100 days, you will be able to slowly cut back on taking the research drug. The research team will give you more detail at that time. If you have GVHD before day +60 post-transplant the research drug will be stopped, and you will continue to take the CsA for 100 days post-transplant. We expect that you will take part in this study for one year after your transplant.

The tests that will be done are shown in the 2 tables on the next page. At each of 6 visits, you will have a physical exam, checked for cancer and for any GVHD signs. Blood is

drawn at each visit and will be about 3 ¼ Tablespoons (T). Your bone marrow will be checked 4 times on this study.

The first table has the tests or exams that would be done for anyone getting a transplant.

STANDARD OF CARE STUDIES	SAMPLE	AMOUNT in (tsp) teaspoons	Before trans-plant	After Transplant				
				MONTH 1	MONTH 2	MONTH 3	MONTH 6	MONTH 12
Pregnancy test	Blood	1/2	X	If needed				
Complete Blood Count.	Blood	up to 1/2	X	every day at first, then weekly			X	X
Chemistry	Blood	up to 1/2	X	Weekly			X	X
Lipid panel	Blood	½				X		
Check for Viruses	Blood	1	X	Weekly			If needed	
Chimerism	Blood	up to 1/2		Weekly upon engraftment			X	X
	Bone Marrow	1/4		X		X		X
MRD	Bone Marrow	1/2	X	X		X		X
White blood cell numbers	Blood	up to 1	X	X	X	X	X	X
Immune system	Blood	1/2	X			X		X
Total CLINICAL blood amounts per time point in teaspoons (tsp)			5 tsp	4 tsp	3 tsp	4 tsp	3 tsp	4 tsp

The tests below are just for this research study.

IMMUNE RESEARCH STUDIES	SAMPLE	AMOUNT in (tsp) teaspoons	Before transplant	After Transplant				
				Day +40	Day +47	MONTH 3	MONTH 6	MONTH 12
CNI60 Lymphocyte Research Lab	Blood	About 3 tsp	X			X	X	X
CNI60 Phenotype Research Lab	Blood	About 1 tsp	X			X	X	X
CNI60 pSTAT 3/5 Assay Research Lab	Blood	About 1 tsp		Pre-Ruxolitinib x1 4 hrs. post-Ruxolitinib x1	Pre-Ruxolitinib x1 4 hrs. post-Ruxolitinib x1			
Total sample volume in teaspoons (tsp)			4 tsp	2 tsp	2 tsp	4 tsp	4 tsp	4 tsp

PK STUDIES	SAMPLE	AMOUNT in (tsp) teaspoons	Day -3	Day -2	Day -1	Day 0	Day +3	Day +7	Day +14	Day +21	Day +40	Day +47	Day +54	Day +61
PK for rATG	Blood	About ½ tsp	x2	x2	x2	x1	x1	x1	x1	x1				
PK for ruxolitinib	Blood	About ½ tsp									x6	x6	x2	x2
Total sample volume in teaspoons (tsp)			1 tsp	1 tsp	1 tsp	½ tsp	1 tsp	½ tsp	½ tsp	½ tsp	3 tsp	3 tsp	1 tsp	1 tsp

- Leftover PK samples from Day +54 and Day +61 will be utilized for pSTAT 3/5 testing (no additional blood draw will be required from the participant).

5. What are the risks and benefits of taking part in this study?

a. Risks

Your risks are mainly related to the transplant and the preparation for it. You could have serious and possibly fatal disorders such as GVHD, stopped up blood vessels, way too many white blood cells, infections, bleeding, anemia, and major problems with sores in your mouth and other mucous membranes.

Side effects of donor cell infusion.

The infusion of donor cells may cause blockage of the blood vessels in the lungs, kidney damage, trouble breathing, or failure of marrow to grow and make normal blood cells. There is also a small risk (less than 1 in 100) that the donor cells may contain a bacteria or virus that could cause an infection. The cell infusion will be checked for bacteria, and if there is any sign of infection, you will be treated with antibiotics.

Risks for infection.

You will have a damaged bone marrow and immune system until the new donor cells have grown and begin to function (engraft). During this time, you will be at risk of infection, which can be life-threatening in 5% to 10% of patients. We will give medicines to reduce this risk. Most infections can be treated with antibiotics. Sometimes an infection cannot be treated. In some cases, patients die of infection.

Graft-versus-host disease.

GVHD is a serious and sometimes deadly side effect which may occur after transplant. GVHD happens when the cells you receive don't "see" your cells as similar to themselves and they attempt to attack and destroy these different cells. People can die from GVHD. The medications we will use in this study will be given in an effort to help prevent GVHD.

Should you decide to take part in this study treatment, you may have an increased risk of developing GVHD as the normal drug used to prevent GVHD, cyclosporine, will be stopped after 60 days rather than the usual 100 days.

Chemotherapy and other conditioning agent related risks:

Common side effects of chemotherapy include nausea, vomiting, hair loss, mouth sores, stomach ulcers, and low blood counts. Low blood counts can mean that you are at a higher risk for infection (which may require antibiotics and hospitalizations), bleeding, and

anemia (weakness and pale skin). This may require blood and/or platelet transfusions. Allergic reactions may occur with any medicine.

A possible late side effect of this study treatment and related medications is therapy-related cancer. The exact risk is not known.

The following pages describe possible side effects specific to each of the agents that you will receive as part of this research study. However, unknown side effects may occur.

Risks of TOTAL BODY IRRADIATION

COMMON, SOME MAY BE SERIOUS In 100 people receiving Total Body Irradiation, more than 20 and up to 100 may have:
• Red or brown discoloration of the skin • Upset stomach or vomiting • Hair loss or thinning • Low blood counts • Decreased growth in the site treated or shorter height than expected • Hormonal problems • Thyroid problems

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Total Body Irradiation, from 4 to 20 may have:
• Secondary cancer

RARE, AND SERIOUS In 100 people receiving Total Body Irradiation, 3 or fewer may have:
• None

Risks of the drug CYCLOPHOSPHAMIDE

COMMON,SOME MAY BE SERIOUS In 100 people receiving Cyclophosphamide, more than 20 and up to 100 may have:
• Infection, especially when white blood cell count is low • Low red blood cell count which may cause tiredness, or may require transfusion • Bruising, bleeding • Blood in urine • Nausea, vomiting, diarrhea, loss of appetite, pain in belly • Sores in mouth which may cause difficulty swallowing • Changes in menstrual period which may decrease the ability to have children • Hair loss, skin changes, rash, change in nails

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Cyclophosphamide, from 4 to 20 may have:
• Fluid around the heart • Damage to the bone marrow (irreversible) which may cause infection, bleeding, may require transfusions • Loss or absence of sperm which may lead to an inability to father children

RARE, AND SERIOUS In 100 people receiving Cyclophosphamide, 3 or fewer may have:
• Damage to the heart or heart failure which may cause shortness of breath, swelling of ankles, cough or tiredness • Swelling of the body including the brain which may cause dizziness, confusion • Damage to the lungs or scarring of the lungs which may cause shortness of breath • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Sinusoidal obstructive syndrome (SOS) which may cause damage to the liver, yellowing of eyes and skin, swelling • Kidney damage which may cause swelling, may require dialysis • A new cancer (including leukemia) resulting from treatment of a prior cancer • Stevens-Johnson syndrome which may cause severe skin rash with blisters and peeling which can involve mouth and other parts of the body

Risks of the drug MESNA

COMMON, SOME MAY BE SERIOUS In 100 people receiving Mesna, more than 20 and up to 100 may have:
• Infection, especially when white blood cell count is low • Nausea, vomiting, constipation • Unpleasant taste • Tiredness • Fever

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Mesna, from 4 to 20 may have:
• Swelling of the body • Shortness of breath • Low red blood cell count which may require blood transfusions • Bruising, bleeding • Pain • Loss of appetite, diarrhea • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Worry • Confusion, dizziness, headache, difficulty sleeping • Increased sweating • Hair loss • Rash

RARE, AND SERIOUS In 100 people receiving Mesna, 3 or fewer may have:
• None

Risks of the drug ANTI-THYMOCYTE GLOBULIN (Thymoglobulin®, rabbit ATG)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Anti-Thymocyte Globulin, more than 20 and up to 100 may have:
• Too much potassium in the blood • Abdominal pain • Constipation • Nausea • Low red blood cell count • Headache • Urinary tract infection • Difficulty breathing • Fever, shivering • Increased blood pressure • Increased heartbeat • Low white blood cell count, which may increase risk of infection • Low platelet count, which may cause bleeding, bruising •

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Anti-Thymocyte Globulin, from 4 to 20 may have:
• Muscle pain • Diarrhea • Worry • Swelling of arms and legs • Sepsis, a life-threatening response to severe infection • Serum sickness, a delayed allergic-like reaction after receiving a medication

RARE, AND SERIOUS In 100 people receiving Anti-Thymocyte Globulin, 3 or fewer may have:
• Anaphylaxis, a severe allergic reaction with low blood pressure, rapid heartbeat, sweating and shortness of breath

Risks of CYCLOSPORINE

COMMON, SOME MAY BE SERIOUS In 100 people receiving Cyclosporine, more than 20 and up to 100 may have:
• Shaking or twitching • Tingling in fingers • Kidney damage • High blood pressure • Risk of infections • Excessive hair growth

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Cyclosporine, from 4 to 20 may have:
• Headache • Liver damage • Gum tissue growth

RARE, AND SERIOUS In 100 people receiving Cyclosporine, 3 or fewer may have:
• Seizures • Allergic Reaction

Risks of the drug RUXOLITINIB

COMMON, SOME MAY BE SERIOUS In 100 people receiving Ruxolitinib, more than 20 and up to 100 may have:
• Swelling • Increased blood pressure • Bruising • Low red blood cell count • Low platelet count • Bacterial or viral infection • Headache • Tiredness • Diarrhea

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Ruxolitinib, from 4 to 20 may have:
• Low white blood cell count • Dizziness • Increased cholesterol which is a type of fat molecule in your blood • Increased triglyceride levels which are a type of fat molecule in your blood • Increase in liver enzymes

RARE, AND SERIOUS In 100 people receiving Ruxolitinib, 3 or fewer may have:
These events were uncommon but have occurred in patients with Myelofibrosis (MF) during ruxolitinib treatment and are potentially serious. • Tuberculosis (TB) has occurred in a small number of patients (less than 1%) with MF who were treated with ruxolitinib, but it is not known whether this was due to MF, ruxolitinib, or other factors that are known to increase the risk of tuberculosis (such as diabetes, bronchitis, asthma, smoking, emphysema, or steroid use). Patients will be screened for TB before transplant. • About one week following interruption or abrupt discontinuation of ruxolitinib, some patients with MF experienced a return of symptoms (such as fatigue, bone pain, fever, itching, night sweats, weight loss, or an enlarged spleen). Hence, ruxolitinib will be tapered slowly over one month. • The effect of ruxolitinib on viral replication in patients with chronic hepatitis B virus is unknown. Patients will be screened for this virus before transplant.

Risks of the drug METHOTREXATE

COMMON, SOME MAY BE SERIOUS In 100 people receiving Methotrexate, more than 20 and up to 100 may have:
• Nausea, vomiting, loss of appetite • Increased risk of sunburn, rash • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Methotrexate, from 4 to 20 may have:
• Fluid around heart • Seizure • Internal bleeding which may cause belly pain, black tarry stool, blood in vomit • Blood clot which may cause swelling, pain, shortness of breath • Severe skin rash with blisters and peeling which can involve mouth and other parts of the body • A new cancer resulting from treatment of a prior cancer • Infection, especially when white blood cell count is low • Bruising, bleeding • Low red blood cell count which may cause tiredness, or may require transfusion • Hepatitis or damage to the liver which may cause yellowing of eyes and skin, swelling • Scarring of the liver • Kidney damage which may require dialysis • Sores in mouth which may cause difficulty swallowing • Diarrhea • Confusion

RARE, AND SERIOUS In 100 people receiving Methotrexate, 3 or fewer may have:
• Scarring of the lungs which may cause shortness of breath • Dizziness

LOSS OF PRIVACY: Very rarely, personal info from your records could be given out by accident. This might make you upset, embarrass you, or affect your ability to get insurance. To prevent this, we:

- Store records apart from names or other personal info
- Only allow members of the study team to see the records
- Store data only on computers that are protected with a password and special software

b. Benefits

There may be no benefit to you. However, it's possible that you may not get as bad of a case of GVHD. Also, this study may help future transplant patients. Blood samples will be drawn to check levels of ruxolitinib and rabbit ATG after they have been given. This will help calculate the right dose for these drugs for future transplant patients. Further, research aimed at looking at the relationship of ruxolitinib and rabbit ATG levels with the suppression of the GVHD activation pathway may be useful to improve prevention of GVHD for future transplant patients. These drugs are commonly used.

6. What are the risks to pregnancy, to an unborn child and to the ability to have children when taking part in this study?

Risks for unborn children: The risks of this treatment to an unborn or nursing child are unknown.

Female Risks: Females in the study must not be pregnant or nursing when they start the study and must not get pregnant during the study. If you think you may have become pregnant during the study, you must tell the researcher right away. If you become pregnant, you will be taken out of the study.

Male Risks: The drugs and radiation used in this research study can damage sperm. You should not father a child while you are participating on this study because the drugs may indirectly affect an unborn child resulting in possible birth defects.

Participants in this study must use effective forms of birth control. The researcher will tell you about the best birth control methods to use during this study. Effective forms of birth control may include birth control pills taken by mouth, condoms, and not having sex. Birth control methods should be continued for 6 months after treatment to avoid pregnancy.

7. Can you stop taking part in this study?

a. Can you change your mind about being in this research study?

You may change your mind about taking part in this research study and stop at any time. This decision will not affect your care or your relationship with your doctor at St. Jude. If available, you may continue to receive routine medical care at St. Jude Children's Research Hospital.

If you change your mind about being in this study, samples or related information that have already been given to or used by researchers will not be returned or removed.

b. Can you be taken out of this study without your consent?

You can be taken out of this study by your research doctor for the following reasons:

- You miss too many appointments
- The study team is unable to contact you after multiple tries
- It is determined that keeping you on the study would be harmful to you
- You need a treatment that is not allowed on this study
- The number of cells needed for your transplant could not be received from your donor
- Your condition gets worse
- New information is learned that will give you a better treatment option.

8. What are your other options?

Taking part in this research study is completely your choice. If you decide to take part in this study, you can change your mind and stop at any time. If you decide not to take part in this study, you may still be able to receive care at St. Jude. You may choose to receive transplant treatment followed by cyclosporine the full 100 days, no treatment or to seek treatment somewhere else.

9. How much will it cost you?

If you have health care coverage, we will bill your health care insurer for all standard of care services, tests, and procedures. Billing your health care insurer impacts your annual deductible and life-time maximum, if any. This may affect your health care coverage to some extent if you go to another health care provider or institution in the future.

At St. Jude, you will not be responsible for or receive bills for co-pays, co-insurance, deductibles, or similar patient-liability amounts, or for the cost of medical care not covered by your health insurer. This includes research-only costs. Research-only tests and procedures (such as optional biopsy or blood samples for biomarker testing) will not be billed to you or your health care insurer.

10. Will you be paid for your time or expenses?

You will not be paid for your time or expenses. Also, your samples and/or information may be sold or used to develop a new product or medical test, which may be sold for profit. If this happens, you will not receive any payments.

11. What if there is a problem?

If you have any questions about this study or if you are injured because of this study, contact Dr. Ashok Srinivasan, at 901-595-3300 right away. If you are injured from being in this research study, St. Jude will offer you reasonable and necessary medical treatment for that injury. If you need more care than St. Jude can provide or if you prefer to seek treatment elsewhere, we will help you find medical care somewhere else. St. Jude may bill your insurance company or other third parties, if appropriate. It is not the hospital's policy to provide payment for other types of costs, such as lost wages, disability, or discomfort if you are injured from being in this study. You are not giving up any of your rights by signing this consent form.

12. How will new findings related to your being in this study be shared with you?

The researcher will tell you of any new information learned during your study participation which might cause you to change your mind about continuing in the study.

13. How will you find out the results of this study?

St. Jude researchers share info with people in studies in many ways including:

- Articles on www.stjude.org
- In newsletters
- In medical or scientific journals
- In the media
- A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by the 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.

Published research results will only describe groups of people who took part in the study. Information that points out a single person will not be in research journals or other reports.

14. Will any genetic tests be done and what are the risks of genetic testing?

As discussed above, we will obtain immune cells during this study. Research blood draws will include some genetic testing. Genetic testing on material obtained from these samples should help us learn how your immune cells work, and ways to improve therapies in the future.

The genetic tests are required and considered research only tests. Results are not reported to you or placed in your electronic medical records. The genetic tests include a partial analysis of genetic material obtained from the samples, and may include whole genome sequencing of tumor cells or normal cells from your body. No direct benefits to participants are expected from these genetic tests.

Risks of Genetic/Genomic Testing

There may be risks to your privacy and the privacy of your relatives from storing your information in a database. Although measures are taken to protect your privacy, we do not know how likely it is that your identity could become re-connected with your genetic and health information, and confidentiality cannot be guaranteed. If your genetic information were re-identified, personal information about you, your health, and your risk of disease could become known to others and potentially used to discriminate against or stigmatize you, your family, or your groups. This could also present unknown risks. We believe the chance that this will happen is very small, but we cannot make guarantees. Your privacy and the confidentiality of your data are very important to us; we will make every effort to protect them.

15. What about privacy and confidentiality?

Privacy

Information from research testing, imaging, and other exams or studies, including genomic and genetic and other sensitive information, is relevant to your health and is placed in your medical record unless it is from a research-only laboratory. When you first registered at St. Jude, you received a copy of the St. Jude Notice of Privacy Practices. It tells how your PHI (protected health information), including research information placed in your medical record, may be used or given to someone outside of the hospital. You have the right to read the Notice of Privacy Practices before you sign this form. It may have changed since you first registered at St. Jude. You can find it at the bottom of every page on the St. Jude internet website: www.stjude.org.

A decision to take part in this research means that you agree to let the research team use and share your PHI with other researchers for purposes of the study explained above. This information will be kept indefinitely. You have the right to see, copy, and ask for changes

to your protected health information that will be used or given out. However, research information may not be seen until the end of the study.

These groups, agencies or people may view your information from your research and medical records:

- Food and Drug Administration (FDA)
- Office of Human Research Protections (OHRP)
- National Institutes of Health (NIH)
- Other government agencies
- Your insurance company and other health benefits plan
- St. Jude Children's Research Hospital Institutional Review Board (IRB)
- Other committees or people involved in overseeing research studies
- Center for International Blood & Marrow Transplant Research (including National Marrow Donor Program – NMDP, and Foundation for the Accreditation of Cellular Therapy – FACT)

Confidentiality

Health information and research data obtained from tumor and normal specimens, such as genetic data, are often shared with the research community using various databases, including those maintained by St. Jude and the federal government. Your data may be stored, shared broadly, and used for future research through the St. Jude Cloud run by St. Jude, the Database for Genotypes and Phenotypes (dbGaP) and the Gene Expression Omnibus (GEO) both run by the National Institutes of Health, and the Sequence Read Archive (SRA). This is to advance scientific discovery and satisfy requirements of organizations that fund research and journals that publish that research. Prior to submitting your data to these databases, it will be de-identified by removing any information that could identify you, such as your name, date of birth, medical record number, and any other information that could link your identity to your data. The only health information included will be your age, diagnosis, and response to treatment. There are two types of databases used for sharing research data. One is a controlled access database, and the other is a public, unrestricted access database. Each is described below.

Controlled access database: Your individual genomic data and health information may be put in a controlled-access database. This means that only researchers who apply for and get permission to use the information for a specific research project will be able to access the information. Your genomic data and health information will not be labeled with your name or other information that could be used to identify you. Researchers approved to access information in the database must agree not to attempt to identify you.

Unrestricted access databases: De-identified summary level information from research studies using your samples, genetic information and health information may be freely available in a public, unrestricted database that anyone can use. Summary-level information about all participants included in a dataset, including you, but not genetic data for each individual, may be shared. This public information will not be labeled with your name or other information that could be used to easily identify you, and the risk of anyone identifying you with this information is very low.

You will not be notified every time your genomic information is used for research. We also do not know what types of future research will be done with genomic data from this study.

16. What about identifiable private information and identifiable biospecimens?

Identifiers will be removed from the identifiable private information or identifiable biospecimens and then the information or biospecimens may be used for future research studies or distributed to other investigators for research studies without additional contact with you.

17. Permission to Use Your Data/Information- Permission/HIPAA

If you sign this document, you give permission to all researchers and their staff at St. Jude Children's Research Hospital to use or disclose (release) your health information that identifies you for the research study described in this form.

The health information that we may use or release for this research includes: all information in your medical record, results of physical examinations, medical history, lab tests, or certain health information indicating or relating to a particular condition.

St. Jude Children's Research Hospital is required by law to protect your health information. By signing this document, you give St. Jude Children's Research Hospital permission to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

If you sign this document, you give St. Jude permission to share your information for future research studies and for the placement of information in databases as described in #15 of this consent form. By signing, you will also give St. Jude permission to put your research information, including testing, imaging, genomic and genetic information, other information and study data, and other sensitive information in your medical record (unless the research information is from a research-only laboratory).

The following entities will receive information:

- St. Jude Institutional Review Boards
- Center for International Blood and Marrow Transplant Research (CIBMTR)

You do not have to sign this informed consent document and give your permission, but if you do not, you may not receive research-related treatment.

Please note that you may change your mind and revoke (take back) this permission at any time. Even if you revoke this permission, St. Jude Children's Research Hospital may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this permission, you must write to:

HIPAA Privacy Officer
St. Jude Children's Research Hospital
262 Danny Thomas Place, Mail Stop 280
Memphis, TN 38105

This permission does not have an expiration date.

18. Further Information and Contact Details for Questions about this Research Study

You are encouraged to ask any questions you wish, before, during or after your treatment. If you have any questions about the study, please speak to your study nurse or doctor, who will be able to provide you with the up to date information about the

drug(s)/procedure(s) involved. If you wish to read the research on which this study is based, please ask your study nurse or doctor.

If there is anything you do not understand, or have any other questions, please contact the researcher listed below.

IF AT ANY TIME DURING THE STUDY YOU HAVE ANY DISCOMFORT OR UNUSUAL SYMPTOMS, OR SIDE EFFECTS, PLEASE CONTACT ANY OF THE DOCTORS LISTED BELOW.

Researcher or Study doctor:

Dr. Ashok Srinivasan
St. Jude Children's Research Hospital
262 Danny Thomas Place
Memphis, TN 38105
Tel: (901) 595-3300

If you require any medical or surgical treatments outside of St. Jude such as with your local doctor or another hospital during this study, please tell your researcher and their team.

You can get more details about your rights for being in this study by calling the St. Jude Institutional Review Board/Research Participant Advocate at 901-595-4644 or 901-595-1139. The Research Participant Advocate is an individual who is not part of the research study team and is available to you to discuss problems, concerns and questions. The Advocate can help you obtain information and can share any input you may have about the research to the research study team.

If you decide you would like to take part in this research study, please read and sign the informed consent document. You will be given a copy of this consent form to keep. A copy of the consent form will be put in your patient notes and one will be put with the study records.

You can have more time to think this over if you are at all unsure.

Thank you for taking the time to read this informed consent document and to consider taking part in this research study.

PARENT/GUARDIAN STATEMENT (Required for participants younger than 18 years):

I have read this document, or it was read to me. I have been encouraged to ask questions and all my questions have been answered. I give my permission for my child to be in this research study.

_____	_____	_____AM/PM
Parent/Legal Guardian Signature	Date	Time (circle one)
_____	_____	_____AM/PM
Parent/Legal Guardian Signature	Date	Time (circle one)

ASSENT DISCUSSION (Required for participants 7-13 years old)

□ The research was explained to the minor participant in age-appropriate terms and the minor verbally agreed to take part in the study.

□ Minor declined to take part in the study. The minor declined for the following reason(s):

_____
___

□ An assent discussion was not initiated with the minor for the following reason(s):

□ Minor is under 7 years of age.

□ Minor is incapacitated.

□ Minor refused to take part in the discussion.

□ Other_____

RESEARCH PARTICIPANT STATEMENT (14-17 years old and Adult Participants 18 years and older):

I have read this document, or it was read to me. I have been encouraged to ask questions and all of my questions were answered. I agree to take part in this research study.

_____	_____	_____AM/PM
Research Participant Signature	Date	Time (circle one)

RESEARCHER/DESIGNEE STATEMENT:

I have explained the research to the participant and his/her parent(s) or legal guardian(s). The research participant and parent(s)/guardian(s) were encouraged to ask questions and all questions were answered to their satisfaction. A copy of this form has been given to the participant or his/her representative.

_____	_____	_____AM/PM
Researcher/Designee Signature	Date	Time (circle one)

_____
Print Name

_____	_____	_____AM/PM
Interpreter (if needed) Signature	Date	Time (circle one)

Research Participants Advocate Statement

I observed the informed consent process. The research study, intervention/observation, risks, benefits, and alternatives were presented to the research participant and/or legal guardian(s). They were encouraged to ask questions, and research team members answered all their questions. The participant/parent(s) indicated that they: 1) understood the information presented; and 2) voluntarily consented/agreed to take part in the research.

_____	_____	_____AM/PM
Research Participant Advocate Signature	Date	Time (circle one)

PLEASE UPLOAD COMPLETED CONSENT FORM TO EPIC

A PHASE II PEDIATRIC STUDY OF A GRAFT-VS.-HOST DISEASE (GVHD) PROPHYLAXIS REGIMEN WITH NO CALCINEURIN INHIBITORS AFTER DAY +60 POST FIRST ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT FOR HEMATOLOGICAL MALIGNANCIES

Note: When we say "you" in this consent, we mean "you or your child." When we talk about research, it can be called a clinical trial, research study, or research protocol.

Key Information

To start, we want to highlight the risks and study requirements that we think you should know before deciding if you want to take part in this research study. If you're still interested, we'll then get into more detail.

A. Why are you being asked to volunteer in this study?
You are being asked to take part in this clinical trial because you have a myeloid based cancer diagnosis that requires a bone marrow transplant.

B. What is the usual approach to this cancer?
When you get a transplant, the transplanted cells will see your body as different and will try to fight your body. The symptoms of this fight can be bad and make you very sick. As a group, the symptoms are called graft-versus-host disease (GVHD for short). The GVHD symptoms can happen just about anywhere in your body. They can happen right away or later. To decrease the chance of getting GVHD, doctors normally give patients a drug cyclosporine A (CsA) until day +100 post-transplant and methotrexate (MTX). CsA is a calcineurin inhibitor (CNI) drug and works in a certain way.

C. Why is this study being done?
Instead of giving you CsA until day +100 post-transplant, your doctors would like to give it until day +60 post-transplant and substitute it with a new drug called ruxolitinib which will be added on day +40 post-transplant. This is because CsA has many side effects which increases risk for complications during transplant. Also, it affects the ability of the donor lymphocytes to kill leukemia cells. Ruxolitinib works in a different way than CsA and is well tolerated. It also does not affect the ability of the donor lymphocytes to kill leukemia cells. We will test the combination of CsA with MTX and ruxolitinib to see if the chance of getting any type of GVHD symptoms decreases. The new drug ruxolitinib is approved by the FDA for treatment of bad cases of GVHD.

D. What will happen if you decide to take part in this study?
To start, you will get the standard (normal) about 6 days of treatment before transplant:
- A drug called thiotepa will be given for once a day intravenously (IV) for 2 days then
- Two drugs named busulfan and fludarabine will be given in an IV once a day for 3 days and then
- A drug named rabbit ATG may be given if you have an unrelated donor for your donor transplant. If so, then you will get the rabbit ATG once a day in an IV for 3 days.

Then, you will get a bone marrow transplant by IV.

To keep the chance of GVHD low, you will get the normal drugs, CsA and MTX by IV. About 12 hours after each dose of MTX you will get another drug, leucovorin, that helps decrease the toxicity associated with MTX. MTX will be given on 4 different staggered days over 11 days. You will continue to receive the CsA for 60 days and then it will be stopped.

You will also take the new drug ruxolitinib starting day +40 post-transplant twice a day by mouth for at least 3 months to decrease the chance of getting GVHD symptoms. We will watch you closely and if you do get any symptoms, find out if they are not as bad as we would normally expect. We expect that you will take part in this study for one year after your transplant.

E. What are the research risks and benefits of taking part in this study?
Your risks are mainly related to the transplant and the preparation for it. You could have serious and possibly fatal disorders such as GVHD, stopped up blood vessels, way too many white blood cells, infection, bleeding, anemia, and major problems with your mucous membranes. As the normal drug of CsA will be stopped early it may increase your risk of GVHD. The new drug ruxolitinib may cause anemia or a decrease in the white cell count. There may be no benefit to you. However, it is possible that you may not get as bad of a case of GVHD. Also, this study may help future transplant patients.

F. How many people will take part in this study?
About 30 people will enroll on this study.

G. What are your options?
   a. Taking part in this research study is completely your choice.
   b. If you decide to take part in this study, you can change your mind and stop at any time.
   c. If you decide not to take part in this study, you may still be able to receive care at St. Jude.
   d. Choose to take part in another research study if available.
   e. You may choose no treatment or to seek treatment somewhere else.

If you are still interested in taking part in this research study, [CNI60], more detail will be provided in the following pages.

Table of Contents

1. Why are you being asked to volunteer for this research study?

You are being asked to take part in this clinical trial because you have a myeloid based cancer requiring a transplant. Please take your time in deciding and feel free to discuss it with your family, friends, and St. Jude's staff. Before you agree, it is important that you read this informed consent document that describes the research study. After you understand the study and if you agree to take part, you will be asked to sign this form. You will be given a copy to keep.

2. Who is sponsoring this study?

This study is being sponsored by St. Jude Children's Research Hospital. The study doctor is Dr. Ashok Srinivasan. He can be reached by telephone at 901-595-3300 if you have questions or concerns about this study.

Dr. Kim Nichols, an investigator of this study, has a financial relationship with Incyte, Inc., a publicly-traded pharmaceutical company providing drug for this study. Your enrollment in this trial and its outcome will not cause Dr. Nichols to receive a financial benefit from Incyte.

3. What is the purpose of this study?

The purpose of the study is to find out if it is safe to stop Cyclosporine A (CsA) early on day +60 rather than continuing until day +100 post-transplant, by substituting it with a new drug called ruxolitinib. We will determine if the new drug ruxolitinib given with cyclosporine and methotrexate is safe and effective in preventing GVHD after a transplant. We will follow your progress for a year after your transplant.

4. What will be done in this study?

You will be in the hospital at first. An IV line will be put in so that conditioning treatments can be given that way. Conditioning is the treatment that gets your body ready to accept the transplant. Your conditioning treatment will begin about 10 days before your transplant. The table below describes the treatment you will receive. The conditioning treatments below is standard of care and used in most transplants. You will also receive treatment to prevent GVHD with CsA and MTX which is standard of care and used in most transplants. In this clinical trial CsA is being discontinued early on day +60 and being substituted by ruxolitinib the new drug on day +40 post-transplant.

Schedule	Medication or Procedure Name
Days -6 and -5	Thiotepa (a chemotherapy)
Days -4, -3 and -2	Busulfan (a chemotherapy)
Days -4, -3 and -2	Fludarabine (a chemotherapy)
Days -3, -2 and -1	Rabbit ATG (an antibody, used only if your donor is not a matched brother or sister)
Day -1	Cyclosporine treatment begins (a treatment to prevent GVHD)
Day 0	Bone marrow infusion
Days +1, +3, +6 and +11	Methotrexate (a treatment to prevent GVHD)
Day +40	*Ruxolitinib treatment begins (a treatment to prevent GVHD)

The minus sign (-) means before your transplant. Day 0 is the transplant day. The plus sign (+) means after your transplant.

**New drug being studied in this clinical trial*

During and after these treatments, we will keep watching you and checking in to see how you are feeling. We will do lots of tests the 28th day (about a month) after your transplant to see if it is taking.

When you are feeling well enough, you will be able to move out of the hospital and into St. Jude housing. You will keep taking cyclosporine daily for 60 days. After you start ruxolitinib on day +40 you will continue taking it twice a day for 100 days post-transplant. We will check you regularly during this time. After 100 days, you will be able to slowly cut back on taking the research drug. The research team will give you more detail at that time. If you have GVHD before day +60 post-transplant the research drug will be stopped, and you will continue to take the CsA for 100 days post-transplant. We expect that you will take part in this study for one year after your transplant.

The tests that will be done are shown in the 2 tables on the next page. At each of 6 visits, you will have a physical exam, checked for cancer and for any GVHD signs. Blood is

drawn at each visit and will be about 3 ¼ Tablespoons (T). Your bone marrow will be checked 4 times on this study.

The first table has the tests or exams that would be done for anyone getting a transplant.

STANDARD OF CARE STUDIES	SAMPLE	AMOUNT in (tsp) teaspoons	Before trans-plant	After Transplant				
				MONTH 1	MONTH 2	MONTH 3	MONTH 6	MONTH 12
Pregnancy test	Blood	½	X	If needed				
Complete Blood Count	Blood	up to ½	X	every day at first, then weekly			X	X
Chemistry	Blood	up to ½	X	Weekly			X	X
Lipid panel	Blood	1/2				X		
Check for Viruses	Blood	1	X	Weekly			If needed	
Chimerism	Blood	up to ½		Weekly upon engraftment			X	X
	Bone Marrow	¼		X		X		X
MRD	Bone Marrow	½	X	X		X		X
White blood cell numbers	Blood	up to 1	X	X	X	X	X	X
Immune system	Blood	½	X			X		X
Total CLINICAL blood amounts per time point in teaspoons (tsp)			5 tsp	4 tsp	3 tsp	4 tsp	3 tsp	4 tsp

The tests below are just for this research study.

IMMUNE RESEARCH STUDIES	SAMPLE	AMOUNT in (tsp) teaspoons	Before transplant	After Transplant				
				Day +40	Day +47	MONTH 3	MONTH 6	MONTH 12
CNI60 Lymphocyte Research Lab	Blood	About 3 tsp	X			X	X	X
CNI60 Phenotype Research Lab	Blood	About 1 tsp	X			X	X	X
CNI60 pSTAT 3/5 Assay Research Lab	Blood	About 1 tsp		Pre-Ruxolitinib x1 4 hrs. post-Ruxolitinib x1	Pre-Ruxolitinib x1 4 hrs. post-Ruxolitinib x1			
Total sample volume in teaspoons (tsp)			4 tsp	2 tsp	2 tsp	4 tsp	4 tsp	4 tsp

PK STUDIES	SAMPLE	AMOUNT in (tsp) teaspoons	Day -4	Day -3	Day -2	Day -1	Day 0	Day +3	Day +7	Day +14	Day +21	Day +40	Day +47	Day +54	Day +61
PK for busulfan	Blood	About ½ tsp	x4	x4											
PK for fludarabine	Blood	About ½ tsp	x3	x1											
PK for rATG	Blood	About ½ tsp		x2	x2	x2	x1	x1	x1	x1	x1				
PK for ruxolitinib	Blood	About ½ tsp										x6	x6	x2	x2
Total sample volume in teaspoons (tsp)			3 ½ tsp	3 ½ tsp	1 tsp	1 tsp	½ tsp	½ tsp	½ tsp	½ tsp	½ tsp	3 tsp	3 tsp	1 tsp	1 tsp

- Leftover PK samples from Day +54 and Day +61 will be utilized for pSTAT 3/5 testing (no additional blood draw will be required from the participant).

5. What are the risks and benefits of taking part in this study?

a. Risks

Your risks are mainly related to the transplant and the preparation for it. You could have serious and possibly fatal disorders such as GVHD, stopped up blood vessels, way too many white blood cells, infections, bleeding, anemia and major problems with sores in your mouth and other mucous membranes.

Side effects of donor cell infusion.

The infusion of donor cells may cause blockage of the blood vessels in the lungs, kidney damage, trouble breathing, or failure of marrow to grow and make normal blood cells. There is also a small risk (less than 1 in 100) that the donor cells may contain a bacteria or virus that could cause an infection. The cell infusion will be checked for bacteria, and if there is any sign of infection, you will be treated with antibiotics.

Risks for infection.

You will have a damaged bone marrow and immune system until the new donor cells have grown and begin to function (engraft). During this time, you will be at risk of infection, which can be life-threatening in 5% to 10% of patients. We will give medicines to reduce this risk. Most infections can be treated with antibiotics. Sometimes an infection cannot be treated. In some cases, patients die of infection.

Graft-versus-host disease.

GVHD is a serious and sometimes deadly side effect which may occur after transplant. GVHD happens when the cells you receive don't "see" your cells as similar to themselves and they attempt to attack and destroy these different cells. People can die from GVHD. The medications we will use in this study will be given in an effort to help prevent GVHD.

Should you decide to take part in this study treatment, you may have an increased risk of developing GVHD as the normal drug used to prevent GVHD, cyclosporine, will be stopped after 60 days rather than the usual 100 days.

Chemotherapy and other conditioning agent related risks:

Common side effects of chemotherapy include nausea, vomiting, hair loss, mouth sores, stomach ulcers, and low blood counts. Low blood counts can mean that you are at a higher risk for infection (which may require antibiotics and hospitalizations), bleeding, and anemia (weakness and pale skin). This may require blood and/or platelet transfusions. Allergic reactions may occur with any medicine.

A possible late side effect of this study treatment and related medications is therapy-related cancer. The exact risk is not known.

The following pages describe possible side effects specific to each of the agents that you will receive as part of this research study. However, unknown side effects may occur.

Risks of the drug THIOTEPA

COMMON, SOME MAY BE SERIOUS In 100 people receiving Thiotepa, more than 20 and up to 100 may have:
• Infection, especially when white blood cell count is low • Low red blood cell count which may cause tiredness, or may require transfusion • Bruising, bleeding • Sores in mouth which may cause difficulty swallowing • Prior viral infection that returns which may cause diarrhea, blindness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Thiotepa, from 4 to 20 may have:
• Bleeding from multiple sites including the brain and depending on the site may cause headache, confusion, belly pain, black tarry stool, or blood in vomit • Damage to the liver which may cause yellowing of eyes and skin, swelling • Severe skin rash with blisters and peeling which can involve mouth and other parts of the body • Seizure • Blood in urine

RARE, AND SERIOUS In 100 people receiving Thiotepa, 3 or fewer may have:
• None

Risks of the drug BUSULFAN

COMMON, SOME MAY BE SERIOUS In 100 people receiving Busulfan, more than 20 and up to 100 may have:
• Low red blood cell count which may cause tiredness, or may require transfusion • Infection, especially when white blood cell count is low • Bruising, bleeding • Diarrhea, nausea, vomiting, loss of appetite • Sores in mouth which may cause difficulty swallowing • Belly pain • Headache • Difficulty sleeping • Worry

COMMON, SOME MAY BE SERIOUS In 100 people receiving Busulfan, more than 20 and up to 100 may have:
• Fever

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Busulfan, from 4 to 20 may have:
• Seizure • Internal bleeding which may cause coughing up blood • Damage to or scarring of the lungs • Damage to the liver • Menopause

RARE, AND SERIOUS In 100 people receiving Busulfan, 3 or fewer may have:
• Fluid around heart • Cancer of bone marrow caused by chemotherapy

Risks of the drug FLUDARABINE

COMMON, SOME MAY BE SERIOUS In 100 people receiving Fludarabine, more than 20 and up to 100 may have:
• Cough • Infection, especially when white blood cell count is low • Bruising, bleeding • Increased risk of unusual infections lasting more than 6 months • Vomiting, loss of appetite • Tiredness, fever • Pain

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Fludarabine, from 4 to 20 may have:
• Damage to organs (brain, lungs, others) which may cause tiredness, changes in thinking or shortness of breath • Low red blood cell count, kidney problems which may cause tiredness, bruising, or swelling • Visual disturbances • Nausea, chills • Feeling of "pins and needles" in arms and legs • Confusion

RARE, AND SERIOUS In 100 people receiving Fludarabine, 3 or fewer may have:
• Coma, seizures (with high doses) • Blindness • Kidney damage which may require dialysis

Risks of the drug ANTI-THYMOCYTE GLOBULIN (Thymoglobulin®, rabbit ATG)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Anti-Thymocyte Globulin, more than 20 and up to 100 may have:
• Too much potassium in the blood • Abdominal pain • Constipation • Nausea • Low red blood cell count • Headache • Urinary tract infection • Difficulty breathing • Fever, shivering • Increased blood pressure • Increased heartbeat • Low white blood cell count, which may increase risk of infection • Low platelet count, which may cause bleeding, bruising •

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Anti-Thymocyte Globulin, from 4 to 20 may have:
• Muscle pain • Diarrhea • Worry • Swelling of arms and legs • Sepsis, a life-threatening response to severe infection • Serum sickness, a delayed allergic-like reaction after receiving a medication

RARE, AND SERIOUS In 100 people receiving Anti-Thymocyte Globulin, 3 or fewer may have:
• Anaphylaxis, a severe allergic reaction with low blood pressure, rapid heartbeat, sweating and shortness of breath

Risks of CYCLOSPORINE

COMMON, SOME MAY BE SERIOUS In 100 people receiving Cyclosporine, more than 20 and up to 100 may have:
• Shaking or twitching • Tingling in fingers • Kidney damage • High blood pressure • Risk of infections • Excessive hair growth

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Cyclosporine, from 4 to 20 may have:
• Headache • Liver damage • Gum tissue growth

RARE, AND SERIOUS In 100 people receiving Cyclosporine, 3 or fewer may have:
• Seizures • Allergic Reaction

Risks of the drug RUXOLITINIB

COMMON, SOME MAY BE SERIOUS In 100 people receiving Ruxolitinib, more than 20 and up to 100 may have:
• Swelling • Increased blood pressure • Bruising • Low red blood cell count • Low platelet count • Bacterial or viral infection • Headache • Tiredness • Diarrhea

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Ruxolitinib, from 4 to 20 may have:
• Low white blood cell count • Dizziness • Increased cholesterol which is a type of fat molecule in your blood • Increased triglyceride levels which are a type of fat molecule in your blood • Increase in liver enzymes

RARE, AND SERIOUS In 100 people receiving Ruxolitinib, 3 or fewer may have:
These events were uncommon but have occurred in patients with Myelofibrosis (MF) during ruxolitinib treatment and are potentially serious. • Tuberculosis (TB) has occurred in a small number of patients (less than 1%) with MF who were treated with ruxolitinib, but it is not known whether this was due to MF, ruxolitinib, or other factors that are known to increase the risk of tuberculosis (such as diabetes, bronchitis, asthma, smoking, emphysema, or steroid use). Patients will be screened for TB before transplant. • About one week following interruption or abrupt discontinuation of ruxolitinib, some patients with MF experienced a return of symptoms (such as fatigue, bone pain, fever, itching, night sweats, weight loss, or an enlarged spleen). Hence, ruxolitinib will be tapered slowly over one month. • The effect of ruxolitinib on viral replication in patients with chronic hepatitis B virus is unknown. Patients will be screened for this virus before transplant.

Risks of the drug METHOTREXATE

COMMON, SOME MAY BE SERIOUS In 100 people receiving Methotrexate, more than 20 and up to 100 may have:
• Nausea, vomiting, loss of appetite • Increased risk of sunburn, rash • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Methotrexate, from 4 to 20 may have:
• Fluid around heart • Seizure • Internal bleeding which may cause belly pain, black tarry stool, blood in vomit • Blood clot which may cause swelling, pain, shortness of breath • Severe skin rash with blisters and peeling which can involve mouth and other parts of the body • A new cancer resulting from treatment of a prior cancer • Infection, especially when white blood cell count is low • Bruising, bleeding • Low red blood cell count which may cause tiredness, or may require transfusion • Hepatitis or damage to the liver which may cause yellowing of eyes and skin, swelling • Scarring of the liver • Kidney damage which may require dialysis • Sores in mouth which may cause difficulty swallowing • Diarrhea • Confusion

RARE, AND SERIOUS In 100 people receiving Methotrexate, 3 or fewer may have:
• Scarring of the lungs which may cause shortness of breath • Dizziness

LOSS OF PRIVACY: Very rarely, personal info from your records could be given out by accident. This might make you upset, embarrass you, or affect your ability to get insurance. To prevent this, we:

- Store records apart from names or other personal info
- Only allow members of the study team to see the records
- Store data only on computers that are protected with a password and special software

b. Benefits

There may be no benefit to you. However, it's possible that you may not get as bad of a case of GVHD. Also, this study may help future transplant patients. Blood samples will be drawn to check levels of ruxolitinib, fludarabine and rabbit ATG after they have been given. This will help calculate the right dose for these drugs for future transplant patients.

Further, research aimed at looking at the relationship of ruxolitinib, fludarabine and rabbit ATG levels with the suppression of the GVHD activation pathway may be useful to improve prevention of GVHD for future transplant patients. These drugs are commonly used.

6. What are the risks to pregnancy, to an unborn child and to the ability to have children when taking part in this study?

Risks for unborn children: The risks of this treatment to an unborn or nursing child are unknown.

Female Risks: Females in the study must not be pregnant or nursing when they start the study and must not get pregnant during the study. If you think you may have become pregnant during the study, you must tell the researcher right away. If you become pregnant, you will be taken out of the study.

Male Risks: The drugs and radiation used in this research study can damage sperm. You should not father a child while you are participating on this study because the drugs may indirectly affect an unborn child resulting in possible birth defects.

Participants in this study must use effective forms of birth control. The researcher will tell you about the best birth control methods to use during this study. Effective forms of birth control may include birth control pills taken by mouth, condoms, and not having sex. Birth control methods should be continued for 6 months after treatment to avoid pregnancy.

7. Can you stop taking part in this study?

a. **Can you change your mind about participating in this research study?**

You may change your mind about taking part in this research study and stop at any time. This decision will not affect your care or your relationship with your doctor at St. Jude. If available, you may continue to receive routine medical care at St. Jude Children's Research Hospital.

If you change your mind about being in this study, samples or related information that have already been given to or used by researchers will not be returned or removed.

b. **Can you be taken out of this study without your consent?**

You can be taken out of this study by your research doctor for the following reasons:

- You miss too many appointments
- The study team is unable to contact you after multiple tries
- It is determined that keeping you on the study would be harmful to you
- You need a treatment that is not allowed on this study
- The number of cells needed for your transplant could not be received from your donor
- Your condition gets worse
- New information is learned that will give you a better treatment option.

8. What are your other options?

Taking part in this research study is completely your choice. If you decide to take part in this study, you can change your mind and stop at any time. If you decide not to take part in this study, you may still be able to receive care at St. Jude. You may choose to receive transplant treatment followed by cyclosporine the full 100 days, no treatment or to seek treatment somewhere else.

9. How much will it cost you?

If you have health care coverage, we will bill your health care insurer for all standard of care services, tests, and procedures. Billing your health care insurer impacts your annual deductible and life-time maximum, if any. This may affect your health care coverage to some extent if you go to another health care provider or institution in the future.

At St. Jude, you will not be responsible for or receive bills for co-pays, co-insurance, deductibles, or similar patient-liability amounts, or for the cost of medical care not covered by your health insurer. This includes research-only costs. Research-only tests and procedures (such as optional biopsy or blood samples for biomarker testing) will not be billed to you or your health care insurer.

10. Will you be paid for your time or expenses?

You will not be paid for your time or expenses. Also, your samples and/or information may be sold or used to develop a new product or medical test, which may be sold for profit. If this happens, you will not receive any payments.

11. What if there is a problem?

If you have any questions about this study or if you are injured because of this study, contact Dr. Ashok Srinivasan at 901-595-3300 right away. If you are injured from being in this research study, St. Jude will offer you reasonable and necessary medical treatment for that injury. If you need more care than St. Jude can provide or if you prefer to seek treatment elsewhere, we will help you find medical care somewhere else. St. Jude may bill your insurance company or other third parties, if appropriate. It is not the hospital's policy to provide payment for other types of costs, such as lost wages, disability, or discomfort if you are injured from being in this study. You are not giving up any of your rights by signing this consent form.

12. How will new findings related to your participation in this study be shared with you?

The researcher will tell you of any new information learned during your study participation which might cause you to change your mind about continuing the study.

13. How will you find out the results of this study?

St. Jude researchers share information with people in studies in many ways including:

- Articles on www.stjude.org
- In newsletters
- In medical or scientific journals
- In the media
- A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by the 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.

Published research results will only describe groups of people who took part in the study. Information that points out a single person will not be in research journals or other reports.

14. Will any genetic tests be done and what are the risks of genetic testing?

As discussed above, we will obtain immune cells during this study. Research blood draws will include some genetic testing. Genetic testing on material obtained from these samples

should help us learn how your immune cells work, and ways to improve therapies in the future.

The genetic tests are required and considered research only tests. Results are not reported to you or placed in your electronic medical records. The genetic tests include a partial analysis of genetic material obtained from the samples, and may include whole genome sequencing of tumor cells or normal cells from your body. No direct benefits to participants are expected from these genetic tests.

Risks of Genetic/Genomic Testing

There may be risks to your privacy and the privacy of your relatives from storing your information in a database. Although measures are taken to protect your privacy, we do not know how likely it is that your identity could become re-connected with your genetic and health information, and confidentiality cannot be guaranteed. If your genetic information were re-identified, personal information about you, your health, and your risk of disease could become known to others and potentially used to discriminate against or stigmatize you, your family, or your groups. This could also present unknown risks. We believe the chance that this will happen is very small, but we cannot make guarantees. Your privacy and the confidentiality of your data are very important to us; we will make every effort to protect them.

15. What about privacy and confidentiality?

Privacy

Information from research testing, imaging, and other exams or studies, including genomic and genetic and other sensitive information, is relevant to your health and is placed in your medical record unless it is from a research-only laboratory. When you first registered at St. Jude, you received a copy of the St. Jude Notice of Privacy Practices. It tells how your PHI (protected health information), including research information placed in your medical record, may be used or given to someone outside of the hospital. You have the right to read the Notice of Privacy Practices before you sign this form. It may have changed since you first registered at St. Jude. You can find it at the bottom of every page on the St. Jude internet website: www.stjude.org.

A decision to take part in this research means that you agree to let the research team use and share your PHI with other researchers for purposes of the study explained above. This information will be kept indefinitely. You have the right to see, copy, and ask for changes to your protected health information that will be used or given out. However, research information may not be seen until the end of the study.

These groups, agencies or people may view your information from your research and medical records:

- Food and Drug Administration (FDA)
- Office of Human Research Protections (OHRP)
- National Institutes of Health (NIH)
- Other government agencies
- Your insurance company and other health benefits plan
- St. Jude Children's Research Hospital Institutional Review Board (IRB)
- Other committees or people involved in overseeing research studies

- Center for International Blood & Marrow Transplant Research (including National Marrow Donor Program – NMDP, and Foundation for the Accreditation of Cellular Therapy – FACT)

Confidentiality

Data from your medical record will be entered directly into a secure study-specific database (Trial Master). This will be completed by the assigned study team member within the BMTCT CRO and will be supervised by the study doctor.

Unique study numbers will be used in place of your name or medical record number. These numbers will be used to identify any data that is released to any person or group outside of the study team. Your name will not be recorded on the data collection forms. The list containing the study number and the medical record number will be kept in a password protected file that only study team members may use.

Researchers and study staff are required by law to report suspected child abuse, threat of harm to self or others, and certain diseases that spread from person to person.

16. What about identifiable private information and identifiable biospecimens?

Health information and research data obtained from tumor and normal specimens, such as genetic data, are often shared with the research community using various databases, including those maintained by St. Jude and the federal government. Your data may be stored, shared broadly, and used for future research through the St. Jude Cloud run by St. Jude, the Database for Genotypes and Phenotypes (dbGaP) and the Gene Expression Omnibus (GEO) both run by the National Institutes of Health, and the Sequence Read Archive (SRA). This is to advance scientific discovery and satisfy requirements of organizations that fund research and journals that publish that research. Prior to submitting your data to these databases, it will be de-identified by removing any information that could identify you, such as your name, date of birth, medical record number, and any other information that could link your identity to your data. The only health information included will be your age, diagnosis, and response to treatment. There are two types of databases used for sharing research data. One is a controlled access database, and the other is a public, unrestricted access database. Each is described below.

Controlled access database: Your individual genomic data and health information may be put in a controlled-access database. This means that only researchers who apply for and get permission to use the information for a specific research project will be able to access the information. Your genomic data and health information will not be labeled with your name or other information that could be used to identify you. Researchers approved to access information in the database must agree not to attempt to identify you.

Unrestricted access databases: De-identified summary level information from research studies using your samples, genetic information and health information may be freely available in a public, unrestricted database that anyone can use. Summary-level information about all participants included in a dataset, including you, but not genetic data for each individual, may be shared. This public information will not be labeled with your name or other information that could be used to easily identify you, and the risk of anyone identifying you with this information is very low.

You will not be notified every time your genomic information is used for research. We also do not know what types of future research will be done with genomic data from this study.

17. Permission to Use Your Data/Information- Permission/HIPAA

If you sign this document, you give permission to all researchers and their staff at St. Jude Children's Research Hospital to use or disclose (release) your health information that identifies you for the research study described in this document.

The health information that we may use or release for this research includes: all information in your medical record, results of physical examinations, medical history, lab tests, or certain health information indicating or relating to a particular condition.

St. Jude Children's Research Hospital is required by law to protect your health information. By signing this document, you give St. Jude Children's Research Hospital permission to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

If you sign this document, you give St. Jude permission to share your information for future research studies and for the placement of information in databases as described in #15 of this consent form. By signing, you will also give St. Jude permission to put your research information, including testing, imaging, genomic and genetic information, other information and study data, and other sensitive information in your medical record (unless the research information is from a research-only laboratory).

The following entities will receive information:

- St. Jude Institutional Review Boards
- Center for International Blood and Marrow Transplant Research (CIBMTR)

You do not have to sign this informed consent document and give your permission, but if you do not, you may not receive research-related treatment.

Please note that you may change your mind and revoke (take back) this permission at any time. Even if you revoke this permission, St. Jude Children's Research Hospital may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this permission, you must write to:

HIPAA Privacy Officer
St. Jude Children's Research Hospital
262 Danny Thomas Place, Mail Stop 280
Memphis, TN 38105

This permission does not have an expiration date.

18. Further Information and Contact Details for Questions about this Research Study

You are encouraged to ask any questions you wish, before, during or after your treatment. If you have any questions about the study, please speak to your study nurse or doctor, who will be able to provide you with the up-to-date information about the drug(s)/procedure(s) involved. If you wish to read the research on which this study is based, please ask your study nurse or doctor.

If there is anything you do not understand, or have any other questions, please contact the researcher listed below.

IF AT ANY TIME DURING THE STUDY YOU HAVE ANY DISCOMFORT OR UNUSUAL SYMPTOMS, OR SIDE EFFECTS, PLEASE CONTACT ANY OF THE DOCTORS LISTED BELOW.

Principal Investigator, Researcher:
Dr. Ashok Srinivasan
St. Jude Children's Research Hospital
262 Danny Thomas Place
Memphis, TN 38105
Tel: (901) 595-3300

If you require any medical or surgical treatments outside of St. Jude such as with your local doctor or another hospital during this study, please tell your researcher and their team.

You can get more details about your rights for being in this study by calling the St. Jude Institutional Review Board/Research Participant Advocate at 901-595-4644 or 901-595-1139. The Research Participant Advocate is an individual who is not part of the research study team and is available to you to discuss problems, concerns, and questions. The Advocate can help you obtain information and can share any input you may have about the research to the research study team.

If you decide you would like to take part in this research study, please read and sign this informed consent document. You will be given a copy of consent form to keep. A copy of the consent form will be put in your patient notes, and one will be put with the research study records.

You can have more time to think this over if you are at all unsure.

Thank you for taking the time to read this informed consent document and to consider taking part in this research study.

PARENT/GUARDIAN STATEMENT (Required for participants younger than 18 years):

I have read this document, or it was read to me. I have been encouraged to ask questions and all my questions have been answered. I give my permission for my child to be in this research study.

_____	_____	_____AM/PM
Parent/Legal Guardian Signature	Date	Time (circle one)

_____	_____	_____AM/PM
Parent/Legal Guardian Signature	Date	Time (circle one)

ASSENT DISCUSSION (Required for participants 7-13 years old)

□ The research was explained to the minor participant in age-appropriate terms and the minor verbally agreed to take part in the study.

□ Minor declined to take part in the study. The minor declined for the following reason(s):

_____
___

□ An assent discussion was not initiated with the minor for the following reason(s):

□ Minor is under 7 years of age.

□ Minor is incapacitated.

□ Minor refused to take part in the discussion.

□ Other_____

RESEARCH PARTICIPANT STATEMENT (14-17 years old and Adult Participants 18 years and older):

I have read this document, or it was read to me. I have been encouraged to ask questions and all of my questions were answered. I agree to take part in this research study.

_____ _____ _____AM/PM
Research Participant Signature Date Time (circle one)

RESEARCHER/DESIGNEE STATEMENT:

I have explained the research to the participant and his/her parent(s) or legal guardian(s). The research participant and parent(s)/guardian(s) were encouraged to ask questions and all questions were answered to their satisfaction. A copy of this form has been given to the participant or his/her representative.

_____ _____ _____AM/PM
Researcher/Designee Signature Date Time (circle one)

_____
Print Name

_____	_____	_____AM/PM
Interpreter (if needed) Signature	Date	Time (circle one)

Research Participants Advocate Statement

I observed the informed consent process. The research study, intervention/observation, risks, benefits, and alternatives were presented to the research participant and/or legal guardian(s). They were encouraged to ask questions, and research team members answered all their questions. The participant/parent(s) indicated that they: 1) understood the information presented; and 2) voluntarily consented/agreed to take part in the research.

_____	_____	_____AM/PM
Research Participant Advocate Signature	Date	Time (circle one)

PLEASE UPLOAD COMPLETED CONSENT FORM TO EPIC