Informed Consent to Participate in Research

DRAFT

Please read this form carefully. If there are words or part of this document that you do not understand, you should ask the research doctor or staff to explain any information that is not clear to you before making a decision whether to participate. Your participation is entirely voluntary. You may choose not to participate and you may withdraw at any time.

The Principal Investigator (the person in charge of this research) or a representative of the Principal Investigator will also describe this study to you and answer all or your questions. Please ask questions about anything that you do not understand.

If you are a parent or guardian of a patient younger than 18 years old and have been asked to read and sign this form, the "you" in this document refers to the patient.

This is a consent form for a research study. This form is to help you decide if you want to participate in this study.

The consent form describes a study for patients with follicular lymphoma who have entered remission from treatment with conventional chemotherapy but the lymphoma has now returned or started growing again. Follicular lymphoma is not curable with standard chemotherapy.

The purpose of this study is to see if this type of transplant called a non-myeloablative transplant can improve your chances of a long-term remission. Both your donor's immune system and the chemotherapy drugs that you receive as part of the transplant will be used against your lymphoma.

This study will give more information to doctors about future treatment choices. In addition:

- You will not be paid to be in this study.
- You or your insurance company will pay for all medical bills for your treatment.
- You will not be charged for research tests.
- You will also face the same risks and benefits as any other transplant patient.

Before you decide to join the study, please read the information below. Feel free to ask questions to understand your rights. It is your choice to take part in this study. You and your doctor will discuss other treatment options if you decide not to be in this study.

1. Name of the Subject ("Study Subject")

2. Title of Research Study

A Phase II Trial of Non-Myeloablative Allogeneic Hematopoietic Cell Transplantation for Patients with Relapsed Follicular Non-Hodgkin's Lymphoma Beyond First Complete Response

3a. Principal Investigator Contact Information

Insert name, affiliation and contact information.

3b. Contact Information for Emergencies After Hours or on Weekends or Holidays

Call (xxx) xxx-xxxx, the in-patient Bone Marrow Transplant Unit. Ask to speak to the Charge Nurse.

4. Sponsors and Source of Funding or Other Material Support

The research in this study is paid for by the National Institutes of Health (NIH). The Blood and Marrow Transplant Clinical Trials Network (BMT CTN) will direct the research study.

Rituximab was donated by Genentech. Genentech also gave some financial support to help pay the costs of this study. Genentech did not plan or design this study, nor will it have a part in analyzing the results of this study.

5. Study Purpose

A conventional allogeneic stem cell transplant is where the patient receives high doses of chemotherapy followed by an infusion of blood stem cells donated by a sibling (brother or sister) or unrelated donor who has the same tissue type (genetically matched). The blood stem cells would rescue your bone marrow from the toxic effects of chemotherapy. However, because the stem cells come from a healthy donor, these blood stem cells also replace your immune system with the donor's immune system. This new immune system also helps fight your lymphoma. This effect of an allogeneic stem cell transplant (SCT) is called a graft-versus-tumor effect. An allogeneic peripheral blood SCT is when a donor's stem cells are collected from his/her blood and then given to you after you receive chemotherapy, also known as conditioning therapy. In some cases the donor stem cells may be frozen before given to you. Unfortunately, the

traditional type of allogeneic SCT that uses high doses of chemotherapy and radiation can have many serious side effects and a high-risk of treatment-related death.

The inability of many lymphoma patients to tolerate a traditional allogeneic SCT may relate to combining the toxic effects of high-dose therapy and the immune effects of the allogeneic SCT. Recent studies have shown that a less toxic type of allogeneic SCT, called a non-myeloablative SCT (also sometimes called a mini transplant or reduced intensity transplant), can more safely be carried out. This lower intensity transplant appears to still control lymphoma. In this study, you will receive this type of transplant and receive lower doses of chemotherapy compared to the doses used in a conventional allogeneic SCT.

The purpose of this study is to determine how effective this non-myeloablative transplant will control and possibly cure your lymphoma. Non-myeloablative SCT has been shown to control your kind of lymphoma.

6. How many people will take part in the study?

As many as 65 patients will take part in this study at different hospitals in the United States.

7. Study Plan

Allogeneic stem cell transplant uses blood stem cells from a brother or sister donor or a matched unrelated donor for the transplant.

- Non-myeloablative SCT uses lower amounts of chemotherapy and radiation than what is used in standard allogeneic transplants.
- After the chemotherapy, the stem cells from your donor will be given to you.
- Your immune system will be replaced by the donor's immune system.
- A non-myeloablative SCT depends on the donor's immune system to destroy the lymphoma cells in your body.

<u>Rituximab Therapy</u>
You also will receive 4 doses of a drug called rituximab. Rituximab is a drug that is not considered chemotherapy but is called a monoclonal antibody. This drug works by attacking only the B cells in your body. B cells are a type of white blood cell in your blood; bone marrow and lymph nodes that normally help fight infection. However, in patients with follicular lymphoma, it is the B cells that become malignant (cancerous) and become lymphoma cells. Rituximab is already commonly used either alone or together with chemotherapy for patients with follicular lymphoma and other types of lymphoma.

You will have blood samples drawn to study the actions of Rituximab in your body. You will have 3-5 mL (about 1 teaspoon) of blood drawn on 5 different days (total of up to 25 mL). The first sample will be taken before the transplant. The remaining samples will be taken after the

transplant at 4 weeks, 3 months, 6 months and 1 year. This blood will be drawn from an existing central venous catheter or a temporary peripheral venous catheter.

8. Procedures and Tests

If you agree to participate in this study, your transplant process will include many steps to:

- Evaluate your health.
- Determine if you have a matched brother or sister donor.
- Prepare your body for a stem cell transplant.
- Receive your stem cell transplant.
- Help your body recover after transplant.
- Measure your health and well being over two years after your transplant.
- Measure your quality of life using surveys before your transplant and two years after your transplant.

If you have a matched brother or sister donor, they will also have a health evaluation, their cells collected for transplant and sign a consent for the study.

If your donor is an unrelated donor, that person will also have the same health evaluation as mentioned above with a sibling donor.

If you have a genetically (HLA) matched brother or sister or a matched unrelated donor, you will have a **non-myeloablative allogeneic SCT**. Your brother or sister or unrelated donor must be willing and able to donate blood stem cells for your transplant.

You will start the **conditioning regimen** also known as the **preparative regimen**. This is done to prepare your body for transplant. The schedule of the preparative regimen is provided in Table 1 if your donor is related to you or in Table 2 if your donor is unrelated to you.

Your doctor will use a combination of three drugs given through your veins:

- **Rituximab** – to lower the number of lymphoma cells, and
- **Cyclophosphamide** – also to lower the number of lymphoma cells and lower the chance of donor stem cell rejection, and
- **Fludarabine** – to lower the chance of donor stem cell rejection.

The purpose of using these drugs with chemotherapy is to weaken your immune system and lower the chance that your body will reject the donated stem cells and to reduce the amount of lymphoma in your body.

You will receive two more drugs during this process to lower the chance of rejecting the donor cells and to lower the chance of developing serious graft-versus-host disease:

- Tacrolimus

- Methotrexate

Graft-versus-host disease (GVHD) is a condition where the donated stem cells attack your skin, liver, intestines and other organs. There is about a 50-60% chance that GVHD will happen after a non-myeloablative allogeneic transplant, but in most cases it is a mild form of GVHD. GVHD can be both helpful and harmful. Mild GVHD may protect against the return of your lymphoma, by attacking the cancer cells. There is approximately a 10-15% chance that serious GVHD may cause organ damage or even death.

Tacrolimus can be taken as a pill or by injection into your vein. Your doctor will decide how you will take it. You will need to take the tacrolimus for at least 6 months. You may need to take it longer if you develop graft-versus-host disease. Methotrexate will be given through your vein for 3 doses on the first, third and sixth day after your transplant **if your donor is your brother or sister**.

If your donor is a matched unrelated donor, you will receive a 4th dose of methotrexate on the 11th day after transplant to decrease the risk of graft-versus-host disease.

TABLE 1: CONDITIONING SCHEDULE FOR NON-MYELOABLATIVE SCT FOR PATIENTS WITH A MATCHED BROTHER OR SISTER DONOR

	Days BEFORE Transplant							
	-13	-6	-5	-4	-3	-2	-1	0*
Fludarabine			✓	✓	✓			
Cyclophosphamide			✓	✓	✓			
Rituximab	✓	✓						
Tacrolimus						✓	✓	daily
Transplant								✓

* You will have your transplant on **"Day Zero (0)."**

	Days AFTER Transplant							
	1	2	3	4	5	6	7	8
Rituximab	✓							✓
Tacrolimus**	✓	✓	✓	✓	✓	✓	✓	✓
Methotrexate	✓		✓			✓		

** Tacrolimus will be given daily for at least 6 months or longer if GVHD occurs

TABLE 2: CONDITIONING SCHEDULE FOR NON-MYELOABLATIVE SCT FOR PATIENTS WITH A MATCHED UNRELATED DONOR

	Days BEFORE Transplant							
	-13	-6	-5	-4	-3	-2	-1	0*
Fludarabine			✓	✓	✓			
Cyclophosphamide			✓	✓	✓			
Rituximab	✓	✓						
Tacrolimus						✓	✓	daily
Transplant								✓

***** You will have your transplant on **"Day Zero (0)."**

	Days AFTER Transplant								
	1	2	3	4	5	6	7	8	11
Rituximab	✓							✓	
Tacrolimus**	✓	✓	✓	✓	✓	✓	✓	✓	✓
Methotrexate	✓		✓			✓			✓[1]

****** Tacrolimus will be given daily for at least 6 months or longer if GVHD occurs
[1] This 4th dose of methotrexate is given if your donor is an unrelated donor.

9. How long will I be in the study?

You will be in the study for up to two years. Follow-up for transplant will last as long as you require care.

10. What are risks of this research study?

You will face risks from the transplant itself, and from treatments given before and after the transplant. Your doctor thinks these risks are less than the risk that you will die from your cancer if it is not treated.

Your heart, lungs, liver, bladder, kidneys, brain or other organs may be damaged by the chemotherapy or by other drugs given to you after the transplant. Rarely, the damage to your organs may be permanent.

Your risk of infection is also increased when undergoing a stem cell transplant. This is due to the chemotherapy that weakens your immune system. Potential infection can be caused by either a bacteria, virus or a fungal organism. Your doctors will monitor you closely for any sign of infection, especially fevers.

There is a risk that your donor's stem cells may not grow after being given to you. This is called graft failure. If graft failure occurs, this may result in low blood counts for a long period of time.

Graft failure can be fatal unless you have a second transplant.

Refer to the Appendix for additional risks and toxicities.

11. What other choices are there if I do not take part in this study?

Participation in this study is entirely voluntary. You are free to refuse to be in the study, and your refusal will not affect current or future health care you receive at this institution. You and your doctor will discuss any other treatment options available to you including:

- Treatment with other drugs or combination of drugs.
- A standard stem cell transplant.
- No therapy directed against your lymphoma at this time, with care to help you feel more comfortable.

12. Are there benefits to taking part in this research study?

You may receive no direct benefits from this study. You may or may not benefit from the scheduled medical assessments required for this study, and extra support from personnel working for this study.

You may be helping other patients get better treatment in the future. A total of 65 patients nationwide will be enrolled on this study. If any new information regarding unexpected side effects are seen in any of the other patients enrolled, you will be informed as soon as possible.

13. What will be done with my blood sample?

A sample (4 teaspoons) of your blood will be collected pre-transplant and stored and used only for research purposes. Usually this blood sample can be collected from you at the time of routine blood collections. If this is not possible, then it would be drawn directly from your central venous catheter.

Your confidentiality will be maintained because no identifying markers (name, etc.) will remain with the sample.

If you agree to allow your blood to be kept for research, you are free to change your mind at any time. We ask that you contact {Principal Investigator} in writing and let him know you are withdrawing your permission for your blood to be used for research. His mailing address is on the first page of this form. Any unused blood will be destroyed.

We will do our best to make sure that your personal information will be kept private and secure. The chance that this information will be given to someone else is very small.

DNA from your stored blood and tissue 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.

You are free <u>not</u> to take part in this additional future research. There will be absolutely no change in your care as a result of your refusal to give these additional samples. Please indicate your choice(s) below:

❑ No, I do not agree to have a blood sample drawn for future research.

❑ Yes, I agree to have blood drawn for future research.

_____ _____

Signature Date

14. What are the costs?

You and/or your insurance company will pay all medical expenses relating to, or arising from stem cell transplantation. Research tests will not be charged to you.

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

15. Will I be paid to take part in this research study?

No.

16. What will happen if I am sick or hurt because of this study?

If you are injured or become ill while taking part in this study, medical care will be provided at this center. No funds have been set aside to pay you if you are injured. You or your insurance company will be charged for ongoing medical care and/or hospitalization.

Contact your doctor or one of the people listed at the start of this form if you are concerned about a research-related injury.

17. Can I change my mind about taking part in this research study?

You may decide to quit this study at any time, for any reason, without notice. However, if you quit after you have had some or all of the treatment but before your transplant, then your blood counts may not return and you could die.

If you decide to quit, we ask that you tell [the Principal Investigator] in writing (his/her address is on the front page of this form). If you do take back your consent, there will be no penalty and you will not lose anything you are entitled to and will continue to receive medical care.

If you have any questions about your rights as a study subject, you may phone the Institutional Review Board (IRB) office at /number/.

18. Can my information still be collected and used if I leave the research study?

If you quit the study, we ask that you let us continue using all information that was already collected. We also ask that you let your doctor continue to tell us about your progress until 5 years after your transplant. You may say no at any time.

19. Can the Principal Investigator remove me from this research study?

You can be taken off the study (with or without your consent) for any of these reasons:

- Staying in the study would be harmful to you.
- You need treatment not allowed in this study.

- You do not follow directions.
- The FDA or study sponsors cancel the study.

20. How will my information be kept private?

The centers and doctors in charge of this study will keep your personal information as private as possible. They will do their best to see that it is shared only when required by state or federal law or the terms of this consent. It is impossible to promise total privacy.

In addition to following state and federal law, the organizations listed below may read or copy your records to make sure the study information is correct. Your research and medical records will have your name on them. They will include things such as your medical history, results of your blood tests and exams, as well as reports about your treatment and office visits. We will do all we can to keep your medical records private. Your name will not be used in any report of study results.

In order to understand the results of the study, people from the /Center Name/ and the Blood and Marrow Transplant Clinical Trials Network (BMT CTN) Data and Coordinating Center (DCC) will need to see medical records with your name on them. These people include:

- Doctors in the study,
- Transplant center committees,
- People (who are not doctors) who check the safety and progress of studies,
- Members of the Institutional Review Board (this committee safe-guards the rights of persons taking part in research), and
- People from the government (the National Institutes of Health and the Food and Drug Administration) might also need to see medical records with your name on them.

Your research and medical records may be shown to these organizations:

- /Institution/
- The National Institutes of Health (NIH)
- Office of Human Research Protection (OHRP)
- The Food and Drug Administration (FDA)
- Institutional Review Board (IRB)
- Data and Safety Monitoring Board (DSMB), not part of /Institution/
- Blood and Marrow Transplant Clinical Trials Network (BMT CTN) Data and Coordinating Center (DCC), including the Center for International Blood and Marrow Transplant Research (CIBMTR), the National Marrow Donor Program (NMDP) and the EMMES Corporation
- The Cancer Trials Support Unit (CTSU), a service sponsored by the National Cancer Institute (NCI) to provide greater access to cancer trials.

- The NCI-sponsored Cooperative Groups that enroll patients on this trial through the CTSU

For questions about access to your medical records, please contact /name / at/number/.

21. How long do you keep my information?

Study records will be kept indefinitely by the transplant center for re-analysis and follow-up.

If you have questions about the keeping of your research records or access to your files, please call /name/at /number/.

22. How will the researcher(s) benefit from your being in this study?

The researchers have no money invested in this study. But, in general, presenting research results helps the career of a scientist. Therefore, the Principal Investigator may benefit if the results of this study are presented at scientific meetings or in the scientific press. In addition, the Principal Investigator is being paid a small amount to cover the cost of performing the study at their Center.

23. HIPAA[1] authorization to use and disclose individual health information for research purposes

a. Purpose: As a research participant, I authorize the Principal Investigator and the researcher's staff to use and disclose my individual health information for the purpose of conducting the research study entitled *Phase II Trial of Non-Myeloablative Allogeneic Hematopoietic Cell Transplantation for Patients with Relapsed Follicular Non-Hodgkin's Lymphoma Beyond First Complete Response*.

b. Individual Health Information to be Used or Disclosed: My individual health information that may be used or disclosed to conduct this research includes: demographic information (e.g., age, date of birth, sex, weight), medical history (e.g., diagnosis, complications with prior treatment), physical examination findings, and laboratory test results obtained at the time of work up and after transplantation (e.g., CT scan, blood tests, biopsy results).

c. Parties Who May Disclose My Individual Health Information: The researcher and the researcher's staff may obtain my individual health information from:

(*list hospitals, clinics or providers from which health care information can be requested)*

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

_____

_____

_____

d. Parties Who May Receive or Use My Individual 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
- Dr. Ginna Laport Study Chairperson, and staff/laboratories at Stanford Hospitals and Clinics
- Staff/laboratories identified in the protocol for the evaluation of other laboratory samples; e.g., TBD for quantitative PCR testing and Covance Laboratories, Inc. for measurement of rituximab blood levels.
- National Heart, Lung, and Blood Institute (NHLBI) and the National Cancer Institute (NCI), both of the National Institutes of Health (NIH), study sponsors
- Blood and Marrow Transplant Clinical Trials Network (BMT CTN), data and coordinating center, including the Center for International Blood and Marrow Transplant Research (CIBMTR), the National Marrow Donor Program (NMDP) and the EMMES Corporation
- 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 research-related treatment that is provided through the study. However, 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.

24. Further Information

If you have further questions concerning this study at any time, you are free to ask your physician whose contact information is available on the cover page of this consent form.

If you have questions regarding your rights as a research participant, you may also contact a representative of the IRB at (XXX) XXX-XXXX.

Dr./Ms./Mr. _____ has explained the above matters to you and you understand that explanation. She/he has offered to answer your questions concerning the procedures involved in this study. You understand the purpose of this treatment as well as the potential benefits and risks that are involved. You have decided to volunteer after reading and understanding all the information on this form. You hereby give your informed and free consent to be a participant in this research investigation. Upon signing this form you will receive a copy.

25. Signatures

As a representative of this study, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this research study; the alternatives to being in the study; and how privacy will be protected:

_____ _____
Signature of person obtaining consent Date

Consenting Adults

The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask the questions I have, and my questions have been answered to my satisfaction. I have been told whom to contact if I have additional questions. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time. I have been told that I will receive a signed copy of this consent form.

Adult Consenting for Self. By signing this form, you voluntarily agree to participate in this study. By signing this form, you are not waiving any of your legal rights.

Signature of Adult Consenting for Self	Date

Parent/Adult Legally Representing the Subject. By signing this form, you voluntarily give your permission for the person named below to participate in this study. You are not waiving any legal rights for yourself or the person you are legally representing. After your signature, please print your name and your relationship to the subject.

Signature of Parent/Legal Representative	Date
Print Name of Legal Representative	Relationship to Participant

Participants Who Cannot Consent But Can Read and/or Understand about the Study

Although legally you cannot "consent" to be in this study, we need to know if you want to take part. If you decide to take part in this study, and your parent or the person legally responsible for you gives permission, you both need to sign. Signing below means that you agree to take part (assent). The signature of your parent/legal representative above means that he or she gives permission (consent) for you to take part.

Assent Signature of Participant	Date

APPENDIX TO PARTICIPANT CONSENT

RISKS AND TOXICITIES RELATED TO A HEMATOPOIETIC CELL TRANSPLANT

There are certain risks related to a blood stem cell transplant. There are risks from the medications and therapy you will receive as part of the conditioning for the transplant and risks related to the transplant itself. Most of these risks and side effects are listed below, but they will vary from person to person. In general, the majority of these side effects are temporary. In rare instances, permanent toxicity may occur.

Likely Side Effects	**Less Likely Side Effects**	**Rare Side Effects**
What it means: This type of side effect may occur in more than 20% of patients. This means that 21 or more patients out of 100 might get this side effect.	What it means: This type of side effect may occur in 20% of patients or less. This means that 20 patients or less out of 100 might get this side effect.	What it means: This type of side effect does not occur very often, but can occur in less than 2% of patients. This means that 1 or 2 patients out of 100 might get this side effect.

Risks Related to the Transplant Conditioning Regimen

Fludarabine: This medication is used in stem cell transplants to reduce the risk of rejecting the donor's transplanted cells.

Likely Side Effects	**Rare Side Effects**
• Lower white blood cell count with increased risk of infection • Lower platelet count with increased risk of bleeding • Anemia (low red blood cell count) • Feeling tired and sleepy	• Nausea (feeling sick to stomach) • Vomiting (throwing up) • Diarrhea (loose stools) • Feeling short of breath • Pneumonia • Numbness and tingling of the fingertips and toes • Difficulty thinking clearly • Trouble seeing or problems with your eyes • Coma

Rituximab (Rituxan): This medication is used to reduce cancer cells. Most side effects occur during the actual infusion of the drug. This typically can happen with your very first infusion of this drug. Your doctor or nurse may need to temporarily slow down or stop the drug infusion until your symptoms lessen.

Likely Side Effects	Less Likely Side Effects	Rare Side Effects
• Shaking chills • Fever • Itching	• Low blood pressure • Shortness of breath • Rash • Nausea/Vomiting • Diarrhea • Headache • Throat irritation • Night sweats • High blood sugar level	• Low blood counts • Tiredness • Pain from areas of lymphoma • Cardiac arrhythmia (abnormal heart rhythm) • Chest pain • Kidney failure • Angioedema (swelling) • Angina (chest pain) • Progressive Multifocal Leukoencephalopathy (PML) (fatal viral infection of the brain)

Common side effects associated with rituximab include a reaction such as fevers chills or shortness of breath during the actual infusion of the drug. A much less common side effect can be a severe allergic reaction called anaphylaxis, which could cause severe shortness of breath, low blood pressure or tightness in your throat. Rituximab can also temporarily cause a low white blood cell count and/or weaken your immune system for up to several months after your last dose of rituximab, which may increase your risk of infection during that time period.

Cyclophosphamide (Cytoxan): This is a common medication used to treat cancer. This medication kills cancer cells by stopping them from growing. Cyclophosphamide may cause you to have diarrhea (loose stools), nausea (feeling sick to your stomach), vomiting (throwing up), short-term hair loss, short-term bladder problems, and, at times, bleeding from the bladder (blood in your urine). A few patients may have bladder damage and bleeding for a longer time. You may be given large amounts of intravenous fluids through your central line to protect your bladder. The central line is placed just prior to receiving the cyclophosphamide (within a few days of the first dose). A bladder catheter (thin plastic tube) may be inserted into your bladder, if your physician thinks that it can help you. Cyclophosphamide slows the making of new blood cells. This causes a risk of infection and/or severe bleeding until the transplanted donor cells begin to work in you. You will get blood transfusions as needed. Cyclophosphamide also lowers your immune (defense) system and as a result you may have more infections. In a small number of patients, cyclophosphamide can damage the heart muscle causing the heart not to pump as well (heart failure). If this occurs you may have shortness of breath and have fluids build-up in your body. Cyclophosphamide can damage the male (testes) or female (ovaries) sex glands. In men, the number of sperm may be reduced. Women who are still menstruating may

have irregular periods or may no longer have any periods. Whether you are a man or woman, this medication may greatly decrease your chances of being able to have a child.

Graft-versus-Host Disease (GVHD)

After the graft begins to function, there is a further risk of a reaction of the graft against your tissues. This reaction is called GVHD and may cause a skin rash, or abnormalities of the liver, or stomach. GVHD may cause nausea (feeling sick to your stomach), vomiting (throwing up), lack of appetite, stomach cramps, diarrhea (loose stools), and bleeding of the gut. Chronic GVHD may occur later after transplantation and may involve problems with the eyes, mouth, lips, throat and liver. Early (acute) or late (chronic) GVHD may become severe enough to result in death. GVHD is treated with drugs that weaken the immune system, and therefore make you more susceptible to infections.

Risks Related to the Medications Used to Help Prevent GVHD

NOTE: These drugs also decrease the risk of rejection of the donor cells.

Tacrolimus: This medication is used to try to prevent GVHD. The immediate side effects you may experience include nausea (feeling sick to your stomach) or vomiting (throwing up) when the medications are given orally. Other side effects you may experience include high blood pressure (hypertension), shaking of the hands (tremor), increased hair growth and possibly an effect on mental function. If you experience these effects they generally go away when the dose of the medication is decreased. A few patients have had a seizure while taking these medications. You may experience a change of liver or kidney function, in which case the medication dose will be reduced or possibly even withheld. In rare cases, the kidney damage caused may require the use of an artificial kidney machine (hemodialysis).

Some patients given tacrolimus develop diabetes and must take insulin while taking tacrolimus.

Methotrexate: This is also a medication used to try to prevent GVHD. Methotrexate causes damage to cells, and therefore can affect many different tissues of your body. It may cause or can worsen the mouth sores or inflammation of the mouth which you may have already developed from the procedures and medications used to prepare you for the transplant. It may also cause nausea (feeling sick to your stomach) and vomiting (throwing up). Methotrexate may slow down the recovery of blood cells after transplantation. Methotrexate can cause kidney damage. If your kidney is already damaged for other reasons, it can worsen kidney function. If kidney damage does occur, the methotrexate dose may be reduced or the mediation may not be given at all.

Tacrolimus, Methotrexate, and Steroids: These medications interfere with the body's defense system (the immune system). This may cause you to have more infections (especially viral infections and pneumonia) for several months after transplant.

Risks and Procedures Related to the Transplant Procedure

The following risks are not specifically related to any one drug or the transplanted donor cells, but they are risks that are a part of the transplant procedure. The following applies to **ALL** patients.

Venipuncture: Although you may require a central venous catheter to donate cells, there may be an occasional need to have an intravenous catheter placed in your arm(s) or you may need to have blood withdrawn from the veins of your arm(s). Drawing blood from the arm may be associated with bleeding into the skin and may very rarely result in an infection.

Central Venous Catheter: A central venous catheter is a flexible sterile tube that can be placed into a large vein either under the collar bone or in your groin area so that blood can be withdrawn. This tube is placed under local anesthesia and will be placed just prior to receiving the cyclophosphamide/rituximab that is given during the cytoreduction process. Complications include blood clots and infection. Clotting may necessitate removal of the catheter or treatment of the clot by injecting a medicine that dissolves blood clots. If you develop an infection, you will require treatment with antibiotics. If the catheter is placed under the collarbone, other uncommon side effects may include swelling of the face and arm and/or lung collapse. If the lung collapses, it may be necessary to place a tube between the ribs to allow the lung to re-expand.

Bleeding: Platelets help your blood to clot. Your platelets will be low until the new bone marrow grows and, as a result, bleeding may occur. This can be minor bleeding, such as nosebleeds or bruising, but more serious, life-threatening bleeding in the lungs, brain and other organs can occur if the platelet count remains low. Usually, there is success in preventing major bleeding problems with transfusions of platelets. However, some patients may not respond well to transfused platelets and may be at serious risk for bleeding.

Mouth Sores and Diarrhea: The chemotherapy causes irritation in the lining of the mouth and intestines. This can result in painful mouth sores and diarrhea and you may need medication to help control the pain. If your mouth sores are severe you may not be able to eat normally until the sores are healed. Mouth sores get better when the white blood count starts to rise.

Capillary Leak Syndrome: This may occur as a result of chemotherapy and radiation therapy. The blood vessels may become 'leaky' and fluid enters the abdominal cavity, lungs, and other tissues. You may gain water weight and not go to the bathroom as often as you normally do. Capillary leak syndrome can be difficult to manage if extra fluid enters the lungs and causes difficulty breathing. You may die if there is continued fluid collection in the lungs.

Unexpected Organ Damage and Other Side Effects: Although your major organs function well, it is possible you may experience unexpected, life-threatening heart, lung, kidney, or liver damage as a result of the transplant. Occasionally, the high doses of chemotherapy cause severe lung damage that cannot always be treated. If this happens, you may need to use oxygen or even a respirator. The lung damage can be life threatening. Rarely, multi-organ failure (such as lung and kidney failure) may occur, which is often fatal.

Late Effects: You may experience side effects that occur several months to many years after your transplant. You may experience poor function of the thyroid gland, requiring you to take thyroid medication. It is rare, but your kidneys could be affected, causing anemia or high blood pressure. There is also a risk you may develop a second cancer including leukemia as a result of the chemotherapy, and/or your lymphoma. If secondary cancers occur they generally do not occur until 10 to 15 years after the transplant but can occur sometimes within five years after transplant. The long-term effects upon heart, lung, and brain are unknown.

Fluid Build-up: You will receive intravenous fluids during the transplant process and you may have difficulty eliminating this fluid. Furosemide is a drug that is often given to help eliminate this excess fluid. This drug may cause hearing loss and loss of body chemicals such as potassium and sodium.

Risk to the Unborn

The treatment that you are undertaking has not been proven to be safe at any stage of pregnancy. Therefore, if you are pregnant or nursing, you are not eligible for this study. Women who have the potential of becoming pregnant must use some form of effective birth control.

Sterility and Future Childbearing Potential for Men and Women

Chemotherapy may cause lasting effects on the reproductive potential of both men and women treated in this manner. It should be emphasized that your cancer treatment/therapy may cause your menstrual periods to become irregular or cease altogether. However, this DOES NOT MEAN THAT YOU CANNOT BECOME PREGNANT, and you must use birth control. It is important that both men and women use birth control while on this study.

Risks Related to the Infusion of Peripheral Blood Stem Cells

The stem cell infusion is given similar to a blood transfusion. The infusion of stem cells usually has few side effects. Rarely the infusion may cause a headache, chest pain or trouble breathing, a slight fever, or blood in the urine. You will be given pre-medications just prior to the infusion to decrease the risk of a reaction. Common, less serious reactions for patients include mild wheezing, mild shortness of breath, back or chest pain or lightheadedness. In rare instances, a severe allergic reaction can occur called anaphylaxis, which could cause a drop in blood pressure or extreme difficulty in breathing. You will be monitored very closely.