PATIENT CONSENT ***IRB #***

Informed Consent to Participate in Research

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. Follicular lymphoma is not curable with standard chemotherapy. Standard stem cell transplants have been used to get patients into remission and improve survival, but the disease still returns.

This study will compare two types of transplants. The purpose is to see if one type of transplant has better results than the other. The study may also find that patients have similar results with either type of transplant.

The results that are important to the study include:

- Blood counts after transplant
- Possible occurrence of infection
- Graft-versus-host disease (GVHD)
- Return of lymphoma
- How long you live after transplant
- Your quality of life

PATIENT CONSENT ***IRB #***

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

Autologous versus Non-Myeloablative Allogeneic Hematopoietic Stem Cell Transplantation for Patients with Chemosensitive Follicular Non-Hodgkin's Lymphoma Beyond First Complete Response or First Partial 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. Sponsor 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.

5. Study Purpose

This study will compare the results from two types of blood stem cell transplant along with the drug rituximab for patients who have follicular lymphoma. The two types of **stem cell transplant (SCT)** that are compared in this study are AUTOLOGOUS SCT and NON-MYELOABLATIVE ALLOGENEIC SCT. Both autologous SCT and non-myeloablative allogeneic SCT have successfully treated this kind of lymphoma.

6. Study Plan

Patients who are able to use matched, donated stem cells from a brother or sister will have an allogeneic non-myeloablative SCT. Patients without a matched brother or sister will have an autologous SCT.

An autologous SCT uses your own stem cells for the transplant:

- Before transplant, your stem cells are collected in a process called leukapheresis, then frozen (or cryopreserved).
- You will have high doses of chemotherapy, with or without radiation, to kill the lymphoma cells in your body.
- The high amounts of chemotherapy and radiation also damage your bone marrow and immune system.
- Your blood stem cells will be given back to you to undo the effects of the chemotherapy.

An allogeneic SCT uses blood stem cells from a brother or sister donor for the transplant. The type of allogeneic transplant used in this study is called a non-myeloablative allogeneic stem cell transplant .

- Non-myeloablative allogeneic SCTs use 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 allogeneic SCT depends on the donor's immune system to destroy the lymphoma cells in your body.

Rituximab Therapy

Whether you receive the autologous or non-myeloablative allogeneic SCT, you also will receive several 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.

7. Procedures and Tests that are Being Done as Part of you Care

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 three years after your transplant.

If you have a matched brother or sister donor, in order for them to participate they will also have a health evaluation and if able to donate their cells collected for transplant and sign a consent for the study.

The treatment will start with **cytoreduction**. Cytoreduction is a process to kill as many lymphoma cells as possible in your body before transplant. All study participants will have cytoreduction before either type of stem cell transplant (autologous or allogeneic non-myeloablative). This process uses **chemotherapy** and rituximab to lower the number of lymphoma cells and another drug, filgrastim (G-CSF) to rebuild your white blood cells:

- **Rituximab** (also called Rituxan) – to lower the number of lymphoma cells,
- **Cyclophosphamide** – also to lower the number of lymphoma cells, and
- **Filgrastim (G-CSF) –** to increase production of healthy white blood cells.

Table 1: Cytoreduction Schedule

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
Rituximab	✓							✓
Cyclophosphamide		✓						
Filgrastim				✓	✓	✓	✓	

If you will be receiving the autologous SCT, you will undergo a procedure called leukapheresis about 12-13 days after receiving the cyclophosphamide. This collects stem cells from your bloodstream as your blood counts recover from the treatment mentioned above. The stem cells are then frozen and stored (cryopreserved). The procedure is explained in more detail at the end of this form.

A) Non-myeloablative stem cell transplant

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

Once your body recovers in about 4 to 6 weeks from the cytoreduction treatment, you will start the **conditioning regimen** also known as the **preparative regimen**. This is done to prepare your body for transplant.

Your doctor will use a combination of two drugs and rituximab 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 this treatment is to weaken your immune system and lower the chance that your body will reject the donated stem cells.

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

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.

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 SCT, 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 in some cases.

Table 2: Conditioning Schedule for Non-myeloablative SCT

	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

B) Autologous stem cell transplant

If you have an autologous stem cell transplant, you will have your own cells collected before the transplant.

Once your body recovers, about 4 to 6 weeks after the cytoreduction treatment, you will start the **conditioning regimen** which is also be called the **preparative regimen**. The conditioning regimen will be chemotherapy based and may include total body irradiation. Whether you receive irradiation in addition to chemotherapy will be determined by your physician and by what preparative regimen is routinely used at your particular hospital/institution. This depends on the doctors at your transplant center. Conditioning is done to prepare your body for transplant. All of the drugs listed below will be given through your veins except the filgrastim, which will be given subcutaneously (injection just under the skin). You will start daily subcutaneous injections of filgrastim starting 5 days after your transplant day to help your white blood cells recover faster.

Your doctor will use:

- **Cyclophosphamide** – to lower the number of lymphoma cells
- **Rituximab** – also to lower the number of lymphoma cells
- **Carmustine or Fractionated Total Body Irradiation** – to lower the number of lymphoma cells
- **VP-16** – to lower the number of lymphoma cells
- **Filgrastim (G-CSF)** – to help your bone marrow make white blood cells after chemotherapy

Only one of the tables below will apply to you. It depends on if you receive total body irradiation plus chemotherapy, or chemotherapy alone. You will have your transplant on **"Day Zero (0)."**

Table 3: Preparative Schedule Using Chemotherapy and Total Body Irradiation

Day	-8	-7	-6	-5	-4	-3	-2	-1	0
	Radiation	Radiation	Radiation	Radiation	VP-16		Cyclopho-sphamide		Transplant

Table 4: Preparative Schedule Using Chemotherapy Only

Day	-6	-5	-4	-3	-2	-1	0
	Carmustine		VP-16		Cyclopho-sphamide		Transplant

Your rituximab maintenance therapy will start about six weeks after your transplant. You will receive 4 weekly doses of rituximab through your veins. The rituximab therapy is to remove any lymphoma cells that may have survived the high dose chemotherapy.

8. What are risks of this research study?

Details of all potential side effects, including those that occur rarely, are discussed in the Appendix.

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

During the cytoreductive phase, the most common complications are fever, chills and shortness of breath during infusion of rituximab, nausea from the cyclophosphamide, and bone pain from the filgrastim. Patients will be at risk for infections and may need transfusions during the 7-14 days when the blood counts are low following this treatment. Those patients who will have stem cells collected may experience temporary numbness or tingling of the fingertips or around the mouth during the blood stem cell collection procedure.

Autologous transplant patients commonly experience some nausea when receiving the chemotherapy or irradiation. Infusion of the stem cells may be accompanied by an unusual taste for a few hours, transient nausea, and occasionally shortness of breath. Nausea, diarrhea and sore throat usually occur about a week after transplantation and lasts for several days. The blood counts are very low for about 2 weeks after transplantation, and during this time, the patient is at high risk for infection and bleeding. Most patients require transfusions of red blood cells and platelets during this time. While the risk of early death following autologous transplant is low, death could occur. The patient may also fail transplant treatment due to relapse of lymphoma.

Allogeneic transplant patients may experience any of the side effects from chemotherapy, drug therapy or cell therapy as listed in the appendix. The patient's blood counts are expected to be low for about 1 week after transplant and this increases the risk of serious and even life-threatening infection. Transfusions of blood and/or platelets and/or intravenous antibiotics may be necessary. There is a possibility that the donor cells will not "take", in other words, not engraft. The period of low blood counts could then be longer but the patient's own marrow function and cell count recovery would be expected to recover. If engraftment occurs, there is about a 50% chance that graft versus host disease (GVHD) will occur. GVHD occurs when the donor’s immune system attacks the patient's organs. The most common organs affected are: 1.) the skin which would result in rash, peeling, and/or deeper injury, 2.) the gut which would cause diarrhea, cramping and possible blood loss, and 3.) the liver which would cause inflammation and/or dysfunction or failure. Medications, including tacrolimus and methotrexate will be given to reduce the risk of acute GVHD. However, if GVHD occurs, additional therapy would be required to treat it. The GVHD might be stopped or it could progress and result in life-threatening medical problems, including late chronic GVHD or possibly death. It is possible that the patient could experience injury to any organ or system as a result of required medications,

transfusions, transplant, and/or other therapies. While the risk of early death following non-myeloablative transplant is low, death could occur. The patient may also fail transplant treatment due to relapse of lymphoma.

9. 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 autologous stem cell transplant.
- A standard or non-myeloablative allogeneic stem cell transplant.
- No therapy directed against your lymphoma at this time, with care to help you feel more comfortable.

10. 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.

11. What will be done with my blood and tissue samples?

Research Blood Samples

Genetic material is any sample of tissue, blood, fluid, etc. obtained from you during the study. With your permission, 10 mL of your blood will be collected prior to the transplant and stored to be used solely for research purposes. The samples will be stored for future studies that will look at responses to treatment based on factors not yet known. These factors may relate to characteristics of your follicular NHL or to how your body tolerated the study treatments. Usually these blood samples can be drawn from you at the time of routine blood collections. Your confidentiality will be maintained because no identifying markers (name, etc.) will remain with the sample.

All BMT CTN research samples will be paired with the respective donor or recipient sample and given unique bar code designations that cannot be linked back to the donor or the recipient. All research samples will become property of the NHLBI after conclusion of the BMT CTN Protocol #0202 study. An NHLBI Biologic Specimen Repository Utilization Committee will advise NHLBI on requests for samples to perform research with these anonymous samples. If an Investigator's request for these samples is approved by the committee, the NHLBI may provide a panel of the specimens requested using unique code numbers. Laboratory test results, clinical information, etc., associated with the coded samples are provided to the Investigator only after

completion of the main protocol. Samples sent to researchers cannot be linked with any remaining sample at the repository.

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.

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:

❑ I agree to have 10 mL of blood collected for future research.

❑ No, I do not agree to have10 mL of blood collected for future research.

_____ _____
Signature Date

12. What if not enough cells are collected to use for transplant?

Your doctor will decide if it is safe to proceed to the planned transplant procedure, depending on how many stem cells are actually collected. The risk of being transplanted with a low number of stem cells is that your blood counts may return to normal levels very slowly or they may stay low permanently. If this occurs, you may need many blood and/or platelet transfusions and/or your risk of infection may increase. If you do not proceed to transplant, your doctor can offer other alternatives such as chemotherapy and/or radiation if he/she feels this is appropriate.

13. 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/.

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

No.

15. 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.

16. 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/.

17. 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.

18. 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 study is cancelled.

19. 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 Marrow Transplant Clinical Trials Network (BMT CTN) Data 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 Coordinating Center (DCC)
- Southwest Oncology Group (SWOG)

Information related to or resulting from your stem cell transplant will be reported to the Center for International Blood and Marrow Transplant Research (CIBMTR). The CIBMTR is a voluntary organization of basic and clinical scientists working together in an effort to gather information on results of stem cell and marrow transplants. This information is used to guide clinical decisions and identify ways to improve transplant outcomes. Scientific data or medical information (not identifiable with you) that could be useful to others may be presented at meetings and/or published in medical journals.

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

20. 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/.

21. 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.

22. 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 *Autologous vs. Non-Myeloablative Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Patients With Chemosensitive Follicular Non-Hodgkin's Lymphoma Beyond First Complete Response or First Partial 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 and Dr. Robert Negrin, Study Chairpersons, 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.
- 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 coordinating center
- Southwest Oncology Group (SWOG), clinical trials cooperative group
- 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.

23. 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.

24. 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 STEM CELL TRANSPLANT

There are certain risks related to a blood stem cell transplant. There are risks from the medications and irradiation (if given) 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.

Risks Related to the Transplant Conditioning Regimen

SECTION A

FOR **ALL** PATIENTS (AUTOLOGOUS AND ALLOGENEIC PATIENTS):

Rituximab (Rituxan): This medication is used to reduce cancer cells. Common side effects associated with rituximab include a reaction such as fevers chills or shortness of breath 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. 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. In people who have ever been infected with hepatitis B virus, there is a risk that the virus can flare up during treatment with drugs that affect your immune system, such as Rituxan. This could lead to liver failure or even death. The risk of hepatitis B virus flaring up may continue for several months after you stop taking Rituxan. If you become jaundiced (yellowing of the skin and eyes) or develop viral hepatitis while taking Rituxan or after stopping treatment, you should tell your study doctor immediately. Your study doctor will discuss this risk with you and explain what testing is recommended to check for hepatitis.

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 will be given large amounts of a sterile solution 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 but you would still be able to have intercourse. 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 will likely greatly decrease your chances of being able to have a child.

Filgrastim (also called G-CSF for Granulocyte Colony Stimulating Factor) : Less than ½ teaspoon (2 mL) filgrastim will be injected under your skin each day and this could cause some minor pain at the injection site. Most people experience varying levels of pain in their bones when treated with this drug which usually feels like muscle aches, bone pain and/or headaches. The pain is usually relieved with acetaminophen (Tylenol™). Aspirin or aspirin-containing drugs must not be taken during filgrastim administration and during leukapheresis without physician approval. A less common side effect is a skin rash. These symptoms go away within a few days after stopping the drug. Other rare potential side effects include signs of allergy such as a rapid heart rate, dizziness, shortness of breath, itching or rash. Temporary changes in laboratory values that monitor liver and bone changes can also occur as well as a temporary increase in your white blood cell count. These return to normal after stopping the drug.

Rarely, people receiving filgrastim have experienced swelling of their spleen and on occasion, internal bleeding from rupture of the spleen. Rupture of the spleen can present as general fatigue and weakness, flank or abdominal pain or loss of consciousness from low blood pressure. Rupture of the spleen can be very serious and is potentially life threatening. Management of this problem could require blood transfusions or surgery. There is less than a 1% chance of this occurring. If you have any unusual symptoms, you should report them immediately.

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.

Veno-Occlusive Disease (VOD): This can occur as a result of high dose chemotherapy, radiation therapy, or both. Veno-occlusive causes severe damage to the liver. Symptoms include jaundice (yellowing of the skin and eyes), weight gain, and extra fluid build-up in the abdominal cavity and other parts of the body. It can often be managed successfully, and completely resolve but can potentially cause death.

Mouth Sores and Diarrhea: The chemotherapy and radiation cause 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 and radiation 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. As a result of radiation, cataracts may occur earlier in life compared to a person who had not had a transplant. If you develop cataracts they may require treatment. 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, radiation 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 and/or irradiation 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.

Risks Related to the Infusion of Bone Marrow or 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. For the autologous patients, some patients react to the preservative called DMSO, which is used in the freezing process of your stem cells. Common, less serious reactions for patients of an autologous or allogeneic SCT 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.

SECTION B

For **AUTOLOGOUS** STEM CELL TRANSPLANT PATIENTS:

VP-16 (etoposide): This is a common medication used to treat cancer. This medication kills cancer cells by stopping them from growing. VP-16 may cause you to have diarrhea (loose stools), nausea (feeling sick to your stomach), vomiting (throwing up), short-term hair loss and skin peeling, especially in the areas of your hands, feet and underarms. VP-16 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. VP-16 also lowers your immune (defense) system and as a result you may have more infections. VP-16 can damage the male (testes) or female (ovaries) sex glands. In men, the number of sperm may be reduced but you would still be able to have intercourse. 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 will likely greatly decrease your chances of being able to have a child.

Total Body Irradiation (applicable to certain patients receiving the autologous SCT): Total body irradiation may cause you to have diarrhea (loose stools), nausea (feeling sick to your stomach), vomiting (throwing up), mouth sores, and painful swelling of the saliva glands for a few days. You may also experience short-term hair loss. Total body irradiation kills both sick and normal marrow, leading to a lack of red blood cells, white blood cells, and platelets. The short-term loss of these blood cells could cause you to become anemic, develop an infection, and/or bleeding. This will continue until the transplanted donor cells begin to work in you. You will get blood transfusions as needed. There is a risk that cataracts (cloudiness) may develop in your eyes. This may mean partial loss of vision, and you may need contact lenses or surgery to remove the cataracts. The total body irradiation dose used will probably result in sterility (not being able to have children) as noted in the cyclophosphamide paragraph on the previous page. It is not known whether the use of total body irradiation will cause more side effects or problems with your health in the future.

Carmustine (also called BCNU) and Etoposide (also called VP-16) (applicable to certain patients receiving the autologous SCT): Side effects from these drugs include nausea (feeling sick to your stomach), vomiting (throwing up), low blood counts, skin rash, diarrhea (loose stools), mouth sores, fevers, and fatigue. Rarely, liver and/or kidney damage can occur. Because of your weakened immune system, a less common side effect is an infection that can be caused either by a bacteria, virus or fungus for which you will be immediately treated with antibiotics. A delayed but less common side effect of the BCNU that can occur about 1-2 months after transplant is pneumonitis or inflammation of your lungs. This can present as a persistent cough, shortness of breath, fevers, persistent fatigue, chest discomfort when taking a deep breath or a sudden decrease in stamina. This would be treated with prednisone. Lung injury from BCNU usually gets better with treatment but some patients have permanent lung damage and some patients die from this side effect.

Leukapheresis: During this procedure, your central venous catheter will be connected to the leukapheresis machine. This machine draws blood out of part of your catheter continuously and filters the stem cells out of your blood stream. The rest of your blood is then returned to your body via another part of your line. Your blood will be thinned with an anticoagulant during the collection procedure to keep your blood from clotting (clogging and thickening) in the tubing and in the machine. This anticoagulant sometimes causes low calcium levels in your blood, which you would feel as temporary numbness or tingling of the fingertips or around the mouth. Should you experience any numbness, you must tell the nurse operating the machine so that oral or intravenous calcium can be given to you. If not corrected, this complication could progress to severe muscle cramps. Other possible unpleasant effects of the collection procedure include lightheadedness, nausea or more rarely, fainting due to temporary lowering of the blood pressure, as well as becoming chilled during the procedure. This procedure takes about 3-4 hours per daily session. Depending on the number of stem cells in your blood, it usually takes 1-3 daily sessions to collect enough stem cells.

SECTION C

For **ALLOGENEIC** STEM CELL TRANSPLANT PATIENTS:

Fludarabine (applicable to patients receiving the allogeneic SCT): This medication is used in stem cell transplants to reduce the risk of rejecting the donor's transplanted cells. Likely side effects you may experience are low white blood cell count with increased risk of infection, low platelet count with increased risk of bleeding, and anemia (low red blood cell count) with tiredness or low energy.

Risk Related Specifically to the ALLOGENEIC Transplant Procedure:

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 Graft-versus-Host Disease (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. Occasionally, 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.

DONOR CONSENT ***IRB #***

Informed Consent to Participate in Research

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.

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.

This is a consent form for a research study. This clinical trial is a research study to determine better treatment for patients with follicular lymphoma.

We invite you to join this study because:

- Your brother or sister has follicular lymphoma
- Your blood stem cells are a match for your brother or sister
- Your brother's or sister's disease may be treated by a blood stem cell transplant, and
- Your brother or sister want to join the follicular lymphoma research study

It is very important for you to know your choices before you decide to join a research study.

Your brother or sister who has low grade follicular lymphoma may be helped by a blood stem cell transplant (SCT). Stem cells are cells found in the bone marrow and blood stream that rebuild your blood, bone marrow and the immune system.

This study uses two sources of blood stem cells for transplant: autologous and allogeneic.

- An **autologous transplant** uses blood stem cells collected from the **patient**.
- An **allogeneic transplant** uses blood stem cells collected from a **brother** or **sister** who are a tissue match with the patient.

Doctors currently use both sources of blood stem cells for transplants. The doctors do not know which type of transplant, autologous or allogeneic, is the better treatment for patients with

follicular lymphoma. Information from this study will help doctors understand the best treatment choices for follicular lymphoma.

We determined that you are a tissue-match to your brother or sister by testing your blood. We tested to see if your antigens matched your brother or sister's antigens. Since all of these antigens matched, your brother or sister is a tissue-match with you. Therefore, your brother or sister has been assigned to receive an allogeneic stem cell transplant.

This consent describes the collection of stem cells from your blood to transplant into your brother or sister. The donation process for stem cells is not experimental. The treatment for your brother or sister is part of a research clinical trial.

This consent form outlines the process, potential risks and benefits of donating your stem cells for transplantation into your brother or sister.

1. Name of the Donor

2. Title of the Research Study

Autologous vs. Non-Myeloablative Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) For Patients With Chemosensitive Follicular Non-Hodgkin's Lymphoma Beyond First Complete Response or First Partial 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. Sponsor and Source of Funding and 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.

5. Study Purpose

You are being invited to participate in this research study because current therapy does not help everyone with follicular lymphoma.

The goal of this clinical research study is to determine whether autologous or allogeneic stem cell transplantation is the better therapy for patients with low grade follicular lymphoma who require a transplant to treat their disease.

You are being asked to donate blood stem cells to your brother or sister because you are a tissue match with them. Donating blood stem cells is not experimental.

6. What will be done if you take part in this research study?

You will undergo a brief medical evaluation and a series of blood tests to prepare for the possible stem cell donation. The following tests and procedures will be done:

- Medical history, physical examination
- Blood tests
- Urine tests
- If you are a woman able to have children, a blood test to check for pregnancy will be done. If you are pregnant, you cannot take part in this study.
- Other tests, such as a chest x-ray or electrocardiogram (ECG or EKG, a picture of the electrical action of the heart) will be done if your physician feels it is necessary.

If your medical evaluation shows any problems or concerns, you will be told about them. This will be kept private and not shared with your brother or sister unless you agree.

Procedures:

Only a small quantity of stem cells is normally present in the blood. A drug called filgrastim, also called G-CSF (granulocyte-colony stimulating factor), can increase the number of these stem cells in the blood. This drug allows enough stem cells to be collected from you for transplantation into your brother or sister.

If the medical exam and blood tests confirm that you are a suitable donor, you will receive injections of filgrastim into the skin (like an insulin injection) once a day for 5 days to help the release of your stem cells into your blood. You must come to the donor center or clinic each day for the filgrastim injections unless these can be arranged at home.

On the fourth and fifth day of filgrastim injections (and possibly the sixth day) you will go to the donor center to have stem cells collected by a machine called a blood cell separator. The procedure of collecting stem cells is called apheresis. Each apheresis procedure takes about 4 to

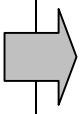
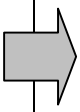
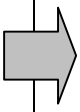
6 hours. The procedure of collecting stem cells involves removing blood from a vein in one arm, passing the blood through the machine where stem cells are collected, and the rest of your blood cells and plasma (the liquid portion of your blood) are returned to you through a vein in your other arm. This procedure will involve placing a needle in each of your arms, collecting the cells over approximately four to six hours during which time you will be required to lie relatively still. If the veins in your arms are not large enough for the needles, you will need to have a temporary central venous catheter placed to collect your stem cells. A central venous catheter is a sterile flexible tube that will be placed into a large vein under local anesthesia. Your physician will explain this procedure to you in more detail and you will be required to sign a separate consent form for this procedure.

Sometimes, not enough stem cells are obtained with two aphereses. If this occurs, you will need to undergo a third apheresis procedure to try to collect enough stem cells.

This process will not remove all of your blood and bone marrow of stem cells. Healthy people have enough stem cells after the collection (aphereses) to make a normal amount of blood cells and the body will replace the lost stem cells with new ones.

You will be weighed and have blood tests (1-2 teaspoons) including a complete blood count before each collection. We repeat the complete blood count after each apheresis procedure.

The following table summarizes the schedule and procedures you undergo when donating stem cells.

DONATION SCHEDULE					
Day 1	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**
 Filgrastim (16 mcg/kg/SQ) injection					You may need to do another day
			 More blood tests done		You may need to do another day
			 (Apheresis) Blood stem cell collection		You may need to do another day
			 Blood cells counted		You may need to do another day

7. **How** long will I be in the study?

You will be in the study for up to a few months from the time you sign the consent until approximately one month after stem cell collection. The actual process of taking filgrastim and then collecting your stem cells though takes less than a week. You will be contacted by phone approximately 30 days after initiation of G-CSF. You will be asked to answer questions about your health since your stem cells were collected.

Your doctor may decide to take your brother or sister off this study if their condition becomes worse, side effects of their treatment are severe or life threatening, or the treatment is no longer in their best interest. If your brother or sister leaves the study there will be no need for you to donate stem cells.

Your doctor may also decide to take you off this study if the filgrastim or if the leukapheresis procedure causes severe, unmanageable or life threatening side effects to you.

You may stop participating at any time. However, if you decide to leave the study, we encourage you to talk to the study doctor first. Leaving the study early may affect your brother or sister's treatment.

8. Will you provide blood samples for research?

Research Blood Samples

Genetic material is any sample of tissue, blood, fluid, etc. obtained from you during the study. With your permission, 3-5 teaspoons from your stem cell collection and 3-5 teaspoons of your blood (taken from your vein) will be collected prior to the recipient's transplant and stored to be used solely for research purposes. The samples will be stored for future studies that will look at responses to treatment based on factors not yet known. Your confidentiality will be maintained because no identifying markers (name, etc.) will remain with the sample.

All BMT CTN research samples will be paired with the respective donor or recipient sample and given unique bar code designations that cannot be linked back to the donor or the recipient. All research samples will become property of the NHLBI after conclusion of the BMT CTN Protocol #0202 study. An NHLBI Biologic Specimen Repository Utilization Committee will advise NHLBI on requests for samples to perform research with these anonymous samples. If an Investigator's request for these samples is approved by the committee, the NHLBI may provide a panel of the specimens requested using unique code numbers. Laboratory test results, clinical information, etc., associated with the coded samples are provided to the Investigator only after completion of the main protocol. Samples sent to researchers cannot be linked with any remaining sample at the repository.

If you agree to allow your stem cells and 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 stem cells and blood to be used for research. His mailing address is on the first page of this form.

DONOR CONSENT ***IRB #***

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. Refusal to participate does not affect your brother or sister's care. Please indicate your choice(s) below:

- ☐ I agree to have blood and stem cells collected prior to the recipient's transplant for future research.
- ☐ No, I do not agree to have blood and stem cells collected prior to the recipient's transplant for future research.

_____ _____

Signature Date

9. What will happen if not enough stem cells are collected from me?

The doctor will decide if it is safe to proceed to the planned transplant procedure, depending on how many stem cells are actually collected. The risk of being transplanted with a low number of stem cells is that your sibling's blood counts will return to normal levels very slowly or they may stay low permanently. If this occurs, he/she may need many blood and/or platelet transfusions and/or the risk of infection may increase. If he/she does not proceed to transplant, the doctor can offer other alternatives such as chemotherapy and/or radiation if he/she feels this is necessary.

10. What are the possible discomforts and risks?

There may be side effects from taking filgrastim and donating stem cells. The filgrastim and leukapheresis may cause some, all or none of the side effects listed below. You should discuss these with your doctor. In addition, there is always the chance of new, unexpected or previously unknown side effects. Other drugs will be given to make side effects less serious and less uncomfortable. Many side effects go away shortly after the filgrastim and leukapheresis is stopped.

Risks and side effects include:

Filgrastim (G-CSF): Less than ½ teaspoon (2 mL) filgrastim will be injected under your skin each day and this could cause some minor pain at the injection site. Most people experience varying levels of pain in their bones when treated with this drug which usually feels like muscle aches, bone pain and/or headaches. The pain is usually relieved with acetaminophen (Tylenol™). Aspirin or aspirin-containing drugs must not be taken during figrastim administration and during leukapheresis without physician approval. A less common side effect is a skin rash. These symptoms go away within a few days after stopping the drug. Other rare possible side effects include signs of allergy such as a rapid heart rate, dizziness, shortness of breath, itching or rash. Temporary changes in laboratory values that monitor liver and bone changes can also occur as well as a temporary increase in your white blood cell count. These return to normal after stopping the drug.

Rarely, normal donors receiving figrastim have experienced swelling of their spleen and on occasion, internal bleeding from rupture of the spleen. Rupture of the spleen can present as general fatigue and weakness, flank or abdominal pain or loss of consciousness from low blood pressure. Rupture of the spleen can be very serious and is potentially life threatening. Management of this problem could require blood transfusions or surgery. There is less than a 1% chance of this occurring. Other, unpredictable side effects may, occur which have not been reported. If you have any unusual symptoms, you should report them immediately.

Possible interactions of figrastim with other drugs have not been fully evaluated; therefore, it is important that you report all drugs, both prescription and non-prescription to your physician. Long-term (beyond one year) safety data on filgrastim administered to normal, healthy people is limited but so far has not identified any late problems for donors.

Leukapheresis; A needle will be placed in each arm. Pain and bruising could occur in both arms, but severe bleeding in the arm is rare. Your blood will be thinned with an anticoagulant during the collection procedure to keep your blood from clotting (clogging and thickening) in the tubing and in the machine. This anticoagulant sometimes causes low calcium levels in your blood, which you would feel as temporary numbness or tingling of the fingertips or around the mouth. Should you experience any numbness, you must tell the nurse operating the machine so that oral or intravenous calcium can be given to you. If not corrected, this complication could lead to severe muscle cramps. Other possible unpleasant effects of the collection procedure include lightheadedness, nausea or more rarely, fainting due to temporary lowering of the blood pressure, as well as becoming chilled during the procedure.

You will lose some blood cells called platelets with the stem cells. These cells help stop bleeding. If your platelet count falls enough to place you in danger of bleeding, (less than 30,000 mL) any further collections will be delayed until your platelet count increases.

Central Venous Catheter; If your arm veins are inadequate (too small) to allow leukapheresis, you will need a central venous catheter to donate cells. 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. Complications include blood clots and infection. Clotting may require 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.

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.

Risks to the Unborn: Since the filgrastim used in this study can affect an unborn baby, you should not become pregnant or father a baby while on filgrastim.

11a. What are the possible benefits to you for taking part in this study?

If you agree to take part in this study, there is no direct medical benefit to you.

11b. What are the possible benefits to others?

The possible benefit to your brother or sister may be improvement in the control of their lymphoma and possibly prolonged survival. We hope the information learned from this study will benefit other patients with lymphoma in the future.

12. If you choose to take part in this study, will it cost you anything?

There is no financial benefit to you by participating in this treatment protocol. Usually, the insurance policy of the stem cell recipient will cover the cost of the donor evaluation and stem cell collection. The transplant coordinator will help you identify insurance coverage before you incur charges for your evaluation and donation. If you have concerns or questions regarding coverage or potential charges, you should contact (contact person's name) at (xxx) xxx- xxxx to review the situation.

13. Will you receive compensation for taking part in this research study?

No.

14. What if you are injured because of the study?

You agree to take the risks listed above. If you experience an injury that is directly caused by this study, only the professional medical care you receive at the [participating clinical facility] will be provided without charge. Hospital expenses will be paid by you or your insurance provider. No other compensation is offered. By signing this form, you have not waived any of your legal rights.

15. What other options or treatments are available if you do not want to be 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 influence current or future health care you receive at this institution.

Instead of being in this study, your brother or sister may have these options:

- Treatment with other drugs or combination of drugs.
- A standard autologous stem cell transplant.
- A traditional allogeneic or non-myeloablative stem cell transplant.
- No therapy at this time, with care to help them feel more comfortable.

Your brother or sister may receive these treatments at this or other centers even if you or they choose not to take part in this study.

16a. How can you withdraw from this research study?

If you agree to be in this study, you are free to change your mind. At any time you may withdraw your consent to be in this study. If you do withdraw your consent, there will be no penalty and you will not lose any benefits to which you are otherwise entitled. If you decide to withdraw, we ask that you notify [Principal Investigator] in writing; his/her mailing address is on the first page of this form.

You must be aware, however, that a decision not to participate once treatment of your brother or sister begins, could have serious harmful consequences for the health of your brother/sister. Not donating stem cells after your brother or sister has received their pre-transplant chemotherapy and/or irradiation may result in his or her death.

If you have any questions regarding your rights as a donor, you may phone the Institutional Review Board (IRB) office at (xxx) xxx-xxxx.

16b. If you withdraw, can information about you still be used and/or collected?

If you withdraw from the study, we will ask your permission to continue using all information about you that has already been collected as part of the study prior to your withdrawal.

16c. Can the Principal Investigator withdraw you from this research study?

Your participation can be withdrawn (with or without your consent) for any of the following reasons:

- You do not qualify to be in the study because you do not meet the study requirements.
- You need a medical treatment not allowed in this study.
- The investigator decides that continuing in the study would be harmful to you.
- The study treatments have a bad effect on you.
- You become pregnant
- Other protocol-specific reasons; for example, if the dose of treatment and/or drugs you have been given has been found to be unsafe.
- The study is cancelled by the National Institutes of Health (NIH) for other administrative reasons.

17. How will your privacy and the confidentiality of your research records be protected?

Study records that identify you will be kept confidential as required by law. You will not be identified by name in the study records. Your records will be assigned a unique code number. The key to the code will be kept in a locked file in the Data Coordinating Center. Authorized persons from [Clinical Center Name], the hospital or clinic (if any) involved in this research, and the Institutional Review Board have the legal right to review your research records and will protect the confidentiality of them to the extent permitted by law. This research study is sponsored and conducted under the authority of the National Institute of Health; therefore, the sponsor and the sponsor's agent also have the legal right to review your research records. Otherwise, your research records will not be released without your consent unless required by law or a court order.

If the results of this research are published or presented at scientific meetings, your identity will not be disclosed.

18. Expiration Date for Retention of Records

The study results will be retained in your research record for at least six years or until after the study is completed, whichever is longer. At that time either the research information not already in your medical record will be destroyed or your name and other identifying information will be removed from such study results. Research information in your medical record will be kept indefinitely.

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

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 scientific journals. In addition, the sponsor is paying the Principal Investigator to conduct this study.

20. 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 *Autologous vs. Non-Myeloablative Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Patients With Chemosensitive Follicular Non-Hodgkin's Lymphoma Beyond First Complete Response or First Partial 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)*

_____

_____

_____

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 and Dr. Robert Negrin, Study Chairpersons, and staff/laboratories at Stanford Hospitals and Clinics

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

- Staff/laboratories identified in the protocol for the evaluation of other laboratory samples; e.g., TBD for quantitative PCR testing.
- 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 coordinating center
- Southwest Oncology Group (SWOG), clinical trials cooperative group
- 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.

21. Further Information

If you have further questions concerning this project at any time, you are free to ask them of Dr._____, who will be available to answer them. His/her telephone number is located on the first page of this consent.

If you have further questions about your disease you are also free to contact The Cancer Information Service of the National Cancer Institute (NCI) using their toll-free number 1-800-422-6237.

22. Signatures

As a representative of this study, I have explained to the donor 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

23. 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. Your 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 Donor Date