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FRED HUTCHINSON CANCER RESEARCH CENTER
UNIVERSITY OF WASHINGTON SCHOOL OF MEDICINE
SEATTLE CHILDREN'S

Consent to Participate in a Research Study Called: Nonmyeloablative Conditioning with Pre- and Post-Transplant Rituximab followed by Related or Unrelated Donor Hematopoietic Cell Transplantation for Patients with Advanced Chronic Lymphocytic Leukemia – a Multi-Center Trial

Who is in Charge of This Research Study?

Principal Investigators: **Fred Hutchinson Cancer Research Center**

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- **What is the purpose of this consent form?**

This form is called a consent form. The purpose of this form is to let you know about a research study being done here at the cancer center. It tells you about the purpose, risks and benefits, and describes what is involved in the study. It also tells you what other choices you have.

- **Do I have to take part in this study?**

No, you do not have to take part in this study. It is up to you. To help you decide if you want to take part in this study, you should:

- Read this form.
- Ask your doctor questions about the study.
- Write down your questions.
- Have your doctor (attending physician) explain anything that you do not understand.
- Discuss it with your family or close friends.
- Take time to think about whether you want to take part in this study.

- **Why is this research study being done?**

The reason for doing this study is to determine whether a new method of stem cell transplant (nonmyeloablative), is useful in treating patients with chronic lymphocytic leukemia (CLL). Nonmyeloablative stem cell transplants use lower doses of chemotherapy and radiation than conventional stem cell transplants. These transplants use stem cells from the blood and appear to be less toxic in other cancers of the blood. Stem cells (both those taken from the donor and those of the recipient) are the "seeds" necessary to make blood cells. We want to see if using less chemotherapy and radiation with drugs that suppress (hold back) the immune system will allow for successful treatment with fewer side effects.

Following infusion of donor stem cells, we hope to see a mixture of the patient's and the donor's stem cells. This mixture of donor and recipient stem cells is called "mixed chimerism." We hope that donor cells will attack the patient's leukemia. This is called the "graft-versus-leukemia" effect. We have added a drug named, Rituximab, which is known to have anti-leukemia activity against CLL cells and has been extensively used for treatment of CLL. We hope the addition of Rituximab will help in controlling CLL early after transplant till the "graft-versus-leukemia" takes control. Further, Rituximab could augment the "graft-versus-leukemia" effect by activating donor immune cells and hence improve disease control. In addition, in the event of recurrence of cancer after this nonmyeloablative transplant, white blood cells from the patient's donor may be given to enhance the graft-versus-leukemia effect, and hopefully remove all remaining cancer cells. There is no guarantee that this procedure will be successful.

- **Why have I been asked to take part in this research study, and who is conducting it?**

You are being asked to take part in this study because you have (CLL), a cancer of the blood that is treatable with a stem cell transplant. Patients in research studies include only those who choose to take part. Please take your time to make your decision. We encourage you to discuss your decision with your doctor, family, and friends. This is a multicenter clinical trial coordinated through the Fred Hutchinson Cancer Research Center in Seattle, Washington.
At the present time there are no curative therapies known outside of stem cell transplantation for your type of cancer. Because of your age or underlying health status, you may have a higher likelihood of experiencing harm from a conventional stem cell transplant.

- **How many people will take part in the study?**

Eighty adult patients with CLL will be enrolled in the study.

- **What is involved in the study?**

Before you begin the study. Before enrollment on the study, you will be checked for suitability for the study. You will be asked to give information about your medical history and undergo the exams and tests listed below. If you have had any of them recently, your doctor may decide not to repeat them. The exams and tests include:

- Bone marrow biopsy & aspiration
- Blood tests
- Urine tests
- Chest x-ray
- Electrocardiogram (ECG)
- MUGA scan or echocardiogram (test to see how well your heart works)
- Pulmonary function tests (test to see how well your lungs work

These exams and tests are not experimental; they are routine. They represent good medical care even if you do not join the study. If you do join, some of these procedures may be done more often than if you were not taking part in the study. The tests may be done on an outpatient basis at your doctor's office or clinic, or in a hospital. If you have no measurable disease at the time of pretransplant staging, bilateral (both sides) bone marrow biopsies will be obtained to assess for minimal residual disease.

During the study: Any significant new findings that develop during the course of treatment, which may affect your willingness to continue participation, will be provided to you. Prior to each treatment you will have a physical exam and blood tests. You will have blood tests at least three times per week to check blood cell counts and kidney function. Other blood tests, including liver function tests, will be done periodically. Blood tests may be required more frequently. In addition, a bone marrow aspiration will be requested at various time points. The bone marrow aspirations will be evaluated for mixed chimerism and disease.

Additional blood samples will be requested for research purposes. We will use your blood and tissue samples for research as described in this consent form. Samples will be stored indefinitely.

We are also trying to determine the best way of dosing rituximab. This study involves collecting blood samples to see how much rituximab is in your body at various times after transplant, so we can understand the best way to give the drug. We will also use simple blood tests to look at two genes which might help us predict how well rituximab will work on your leukemia cells.

Sample	Sample Size	Timing
Blood	Up to 10 ml to 20 ml (approximately 4 teaspoons)	Before and after transplant, and after you return home at approximately Day +10, +24, +38, +60, +84, +180, and one year. These samples will be requested at the same time as your regularly scheduled doctor visits.

If we want to use your tissue in the future for a purpose not described in this consent, we must first send a request to the Institutional Review Board (IRB) for review and approval for all proposed new research.

Procedures that are being tested during the study.

1. Low dose treatment and stem cell transplantation. Peripheral blood stem cells will be used in this study. Peripheral blood stem cells are collected from the blood after the donor has been treated with a drug called growth factor. These cells are then infused into you like a blood transfusion. Treatment is the chemotherapy and radiation necessary to establish a graft, that is, to allow donor stem cells to grow in the recipient's marrow for the production of blood cells.

   We intend to suppress (hold back) your immune system using low dose total body irradiation (TBI) and fludarabine (please see below for side effect profile of these treatments) to allow your body to accept the donor stem cells. Rituximab will be used to control CLL early after transplant till the "graft-versus-leukemia" takes control. Further, Rituximab could augment the "graft-versus-leukemia" effect by activating donor immune cells and hence improve disease control. The immune suppressing drugs cyclosporine (CSP) and mycophenolate mofetil (MMF) will be given after the infusion of donor stem cells to ensure continued acceptance of your immune system to the presence of donor stem cells and to prevent graft-versus-host disease (GVHD). Since the treatment appears to have few serious side effects, we plan for most of your post-transplant course to occur as an outpatient. However, about one-half of patients require admission at some point after transplant. The average hospital stay is approximately 11 days. Listed below is a table that shows the schedule for receiving fludarabine, TBI and the immune suppressing drugs CSP and MMF. Days with a minus sign before them indicate the number of days before the transplant. Days with a plus sign before them indicate the number of days after the transplant.

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Day number	-4	-3	-2	-1	0	+1	+10	+24	+27	+38	+40	+56	+96	+100	+180
Fludarabine	X	X	X												
TBI					200 cGy										
Rituximab		X					X	X		X					
Stem cell infusion					Infusion										
CSP for related		Start	→	→	→	→	→	→		→	→	Taper[A]	→	→	Stop
CSP for unrelated		Start	→	→	→	→	→	→		→	→	→	→	Taper[B]	Stop
MMF for related					Start[C]	→	→	→	Stop						
MMF for unrelated					Start[C]	→	→	→	→	→	Taper[D]	→	Stop		

2. *Molecular Test of Disease Response:* Certain blood cancers can be monitored by a special test that detects the DNA of the tumor cells. This test is called a polymerase chain reaction or PCR test. This sensitive test may be used for monitoring the response of your cancer to the stem cell transplant. This test will be performed using peripheral blood and bone marrow samples. This test will not add to the frequency of standard blood or bone marrow tests scheduled to monitor the response of the leukemia to the stem cell transplant. Some of these tests are still experimental and, therefore, the results of the unapproved tests will not be used for clinical decision making and will not be routinely made available to the patient.

3. *Molecular Test of Donor Engraftment:* The percentage of donor cells in your blood and marrow can be monitored by special tests (e.g. PCR) that detect the DNA of the donor cells. These sensitive tests are used for evaluating the degree of donor engraftment after the blood stem cell transplant. This test will be performed using peripheral blood and bone marrow samples. This test will not add to the frequency of standard blood or bone marrow tests.

4. *Tests to Study the Recovery of the Immune System:* Up to 10mls of blood (less than 1 tablespoon) will be drawn up to 5 times within the first year post-transplant to determine how the immune system has recovered.

- **How long will I be in the study?**

Your treatment will last approximately 3 and 1/2 months, but could be longer. You will be asked to return for follow up at 6 months and every year thereafter. We would like to keep track of your medical condition for the rest of your life to look at the long-term effects of the study. However, you may be taken off the protocol if one of the following happens:

- The study treatment does not work for your cancer;
- You develop a serious side effect that you cannot tolerate or that cannot be controlled with other medications;
- Your health gets worse;
- You are unable to meet the requirements of the study (for example, you cannot take the medicine as prescribed or you refuse follow-up);
- You start other treatments for your cancer;

- Other treatments for your cancer become available;
- Your request;

Your decision to participate in this study is voluntary. You may decide not to participate in this study at any time, for any reason, without notice. However, early withdrawal from treatment during the conditioning regimen without subsequent stem cell transplantation could be fatal. The early discontinuation of the immune suppressing drugs, MMF and Cyclosporine, after blood stem cell transplant could lead to rejection of the donor blood stem cells or life threatening GVHD. We request that you discuss your decision with your primary doctor and if you wish the research physician prior to discontinuing the study.

➢ What is long-term follow-up?

We would like to keep track of your medical condition and health for the rest of your life to look at the long-term effects of the study. Long-term follow-up includes getting information useful for your medical care and research. Results of tests that are done after one year, as needed, help your referring physician plan your future care. We also get information for research by mailing questionnaires to you. The questionnaires will ask how you are doing and if you have any health problems. Research information is entered into our research database.

➢ What are the risks of the study?

There are risks involved in this study, and there may be side effects. Most of these are listed below, but they will vary from person to person. Your doctor may be able to give you other medications to make some of the side effects less bothersome.

Side effects that we know about now are described in the table. Side effects are categorized into either:

- **Likely side effects:** Side effects that may occur in 10% or more of patients (this means that 10 or more patients out of 100 might get this). Certain side-effects in this category could occur in virtually all patients.
- **Less likely side effects:** Side effects that may occur in 3-9% of patients (this means that 3 to 9 patients out of 100 might get this).
- **Rare side effects:** Side effects that do not occur very often, but may occur in less than 3% of patients (this means that 1 or 2 patients out of 100 might get this).

With any drug or combination of drugs, there may be complications or side effects that we do not know about.

Likely Side Effects	*Less Likely Side Effects*	*Rare Side Effects*
Graft-versus-host disease	Allergic reaction (including itching, hives, flushing, hypersensitivity, shortness of breath, wheezing, chest tightness, skin rashes, fever, chills, muscle stiffening, severe breathing problems)	Sores in mouth and/or throat
Nausea	Jaundice (yellowish discoloration of sclera)	Hair loss
Vomiting	Rejection/graft failure	Skin or nail discoloration
Diarrhea	Fluid retention (bloating or swelling)	Nail changes
Loss of appetite	Weakness	Painful burning on the skin of the hands and feet
Fever	Fatigue	Irregular menses or stopping of menses
Lowered white blood cell counts (may lead to infection)	Seizure	Infertility (inability to have children) in women or Sterility for men
Lowered platelet counts (may lead to bleeding)	Tremor	Failure of heart function
Lowered red blood cell counts (may lead to anemia, fatigue, shortness of breath)	Muscle or joint pain	Failure of liver function
Infection		Failure of brain function
		Impairment or failure of kidney function
		Failure of lung function

Stem Cell Transplant. Based on our preliminary studies of patients with various blood cancers, we expect the proposed nonmyeloablative stem cell transplant to be associated with fewer side effects than are observed with a conventional, high-dose radiotherapy and/or chemotherapy, transplant. It is possible that you could experience serious side effects similar to those that occur after conventional stem cell transplants that use high doses of chemotherapy and radiation. These side effects include low blood counts, infections, bleeding, and failure of donor stem cells to grow. Supportive care with red blood cell and platelet transfusions and antibiotic therapy may be necessary. Organ damage may also occur as a result of radiation or treatment with drugs that suppress the immune system. Although one of the goals of this study is to reduce the risk of transplant, the side effects of treatment can be severe enough to cause your death.

For patients receiving unrelated transplants there is an extremely low risk that for reasons beyond our control either (i) your unrelated donor will be unable to donate stem cells or (ii) the donation will result in a product that cannot be infused safely. If either of these extremely unlikely events were to occur after you receive the conditioning regimen, there is a chance that your own

marrow cells will not recover. If your own marrow cells do not recover, the only way to prevent your death would be to find a replacement donor. Finding a replacement donor soon enough to prevent death would be very difficult. Even if another donor is found, the transplant using the replacement donor's stem cells might not be successful.

Graft-versus-host disease (GVHD), or inflammation of the skin, liver, and gastrointestinal tract (usually of acute onset and short duration) due to donor white blood cells, may occur and require treatment with drugs to suppress the immune system. In similar studies, 57% of patients required treatment for GVHD that developed within the first 100 days after transplant. One-half of patients developed a chronic form of GVHD (gradual onset and long duration) that required treatment. Seven percent of patients developed GVHD that was fatal. Severe GVHD and the treatment of GVHD may be associated with life-threatening infection.

Rejection of the Graft. There is a small but possible risk that you will reject your donor's stem cells after transplant. In similar studies of nonmyeloablative transplant following fludarabine and total body irradiation, 3% of patients had rejection. If this occurs, the dose of chemotherapy and radiation given would not be expected to cause a long period of low blood counts, and you would be expected to recover your blood counts if they were relatively normal before the transplant. Although most patients' blood counts will recover, there is a small chance that blood counts may not recover. Failure to recover blood counts following rejection increases the risk of infection or bleeding which may result in death.

Relapse/Disease Progression. The malignancy may not regress or may recur even if the transplant is initially successful. The rate of relapse may be increased compared to conventional transplants that utilized high dose chemotherapy. You will be monitored closely for evidence of relapse or progression of your CLL. Donor lymphocyte infusion and/or other therapies may be performed if your CLL progresses.

Total Body Irradiation (TBI) at high doses in conventional transplants may cause nausea, vomiting, diarrhea, temporary hair loss, and painful swelling of the parotid gland (a gland under the chin) for a few days. TBI may also cause damage to the lining of the mouth, called "mucositis" that requires pain medication and temporary administration of fluids and nutrition by vein. TBI may cause diarrhea that lasts for a few days. In addition TBI can cause damage to the lungs and often causes the formation of cataracts many years after its administration. High dose TBI also destroys normal bone marrow cells in addition to malignant cells. The dose of TBI used in this protocol is approximately one-sixth of that used in conventional transplant protocols, and severe acute side effects have not yet been observed. TBI has been associated with causing infertility; however, it is expected that the risk of infertility will be lower than the risk after transplants that use higher doses of TBI. Although TBI can theoretically cause abnormalities in children born to transplant survivors, the incidence of genetic abnormalities has not been reported to be greater than the general population. However, this is a potential risk and birth control should be used for at least one year after transplant to minimize risks of conceiving. There is a risk that a small percentage of patients may develop a secondary cancer resulting from this treatment. There may be some unknown consequences to the patient's health resulting from the administration of total body irradiation.

You will also be receiving diagnostic exams (CT scans, chest x-rays, bone scan, etc) to help follow your progress. These exams will result in a radiation dose to you, but these doses are

small in comparison to the therapy dose you will receive. They are not expected to increase your health risk.

Fludarabine is a chemotherapy drug used in the treatment of blood cancer. You have received this medicine or one like it in the past as a treatment for your CLL. The fludarabine in this study is not intended to treat your CLL. Fludarabine is being used in stem cell transplants to try and reduce the risk of graft rejection. Its main side effects include lowering of blood counts and increasing the risk of developing infections. In early studies, some patients who received high doses experienced nerve damage; however, such side effects would not be expected with the doses used in this study. Hemolytic anemia (immune damage to red cells) has occurred in some patients with chronic lymphocytic leukemia who received fludarabine. If you have experienced this side effect in the past, there is a possibility that you may again experience severe hemolytic anemia when given fludarabine. All possible medical precautions will be taken to ensure your safety.

Mycophenolate Mofetil (MMF): MMF is a drug used for suppressing the immune system for stem cell transplantation. The drug is reasonably well tolerated by patients who have had nonmyeloablative transplants. There are a small number of patients who have received solid organ transplants and had reversible fall in their red cell or white cell count while receiving MMF. Additionally, cases of Pure Red Cell Aplasia (PRCA) have been reported in some patients receiving MMF. PRCA is a condition in which the bone marrow stops producing red blood cells. In some instances, PRCA can be reversed by reducing or stopping MMF. Your blood counts will be monitored closely and if significant decrease is noted, dose adjustments or stopping your MMF may be indicated.
Cases of progressive multifocal leukoencephalopathy (PML) have occurred in some patients receiving MMF. PML is a rare disorder that affects the central nervous system, and is most often found in patients with suppressed immune systems. It occurs when the polyomavirus (or JC virus) is activated, and can cause neurologic symptoms including weakness on one side of the body, lack of emotion, confusion, cognitive difficulties, and loss of coordination. It can cause permanent disability and is sometimes fatal. You should notify your doctor immediately if you develop any of the above symptoms.
Other uncommon, though potentially important, side effects include nausea, vomiting, diarrhea, and abdominal discomfort. Occasional cases of gastrointestinal bleeding have also been reported among patients receiving MMF for long periods of time.

Likely Side Effects	Less Likely Side Effects	Rare Side Effects
• Nausea (feeling sick to stomach)	• Vomiting (throwing up) • Diarrhea (loose stools) and abdominal discomfort • Lower red blood cell count that is reversible • Lower white blood cell count with increased risk of infection	• Stomach and bowel bleeding (blood in stools) • Secondary cancers

MMF has caused birth defects in humans. The United States Food and Drug Administration (FDA) requires that women who take part in this study must use two forms of contraception if they are fertile and not abstinent.

FOR WOMEN WHO COULD BECOME PREGNANT: Birth defects could occur if you take MMF while you are pregnant. As discussed above, you must use 2 effective forms of contraception if you are fertile and sexually active. You should talk to your doctor to find out which methods of birth control would be most effective for you. You must notify your doctor and the coordinating center for the study immediately if you become pregnant while you are taking MMF. You should not breast feed while you are taking MMF.

Rituximab is a drug made up of an antibody produced in a laboratory. This antibody attaches to a protein on the surface of lymphoma cells and can lead to their destruction. Rituximab can also destroy some normal white blood cells called B-lymphocytes. Rituximab is widely used to treat lymphoma, and you have likely already received it during your earlier treatment. We are studying whether additional doses of rituximab will increase the success of your transplant.

Some patients have an allergic reaction when they receive rituximab. These reactions are generally worst with the first few doses, and may go away with subsequent dosing. We use drugs like diphenhydramine (Benadryl) to prevent such allergic reactions, though they are not always successful. The most common side effects of rituximab are allergic, and include temporary fever, chills, and skin rash. Since rituximab can affect normal lymphocytes, it may increase the risk of certain infections; you will be screened and monitored closely for these infections after your transplant, and you will receive preventive medication against certain infections as part of standard transplant care. In rare cases, rituximab has been associated with bowel injuries or with a disease called progressive multifocal leukoencephalopathy (PML), both of which can be serious, life-threatening, or fatal.

Cyclosporine (CSP) is a drug used for suppressing the immune system. The immediate effects of this drug may include nausea or vomiting when given orally. Other possible side effects include developing high blood pressure (hypertension), shaking of the hands (tremor), increased hair growth, and an effect on mental function. These effects are generally reversible upon decreasing the dose of the drug. An occasional patient has had a seizure, but it is unclear whether CSP, alone or in combination with other drugs, was responsible. There is a risk that a small percentage of patients may develop a secondary cancer resulting from this treatment.

Some patients given intravenous CSP for the treatment of GVHD have experienced a painful sensation in the hands or feet or both. The pain subsided with slowing of the infusion, the improvement of the GVHD or when the CSP was switched from the intravenous to the oral form. Patients may experience a change of liver or kidney function, in which case, the dose of CSP may need to be reduced or possibly withheld. This effect on the kidneys appears to increase when other drugs that might cause kidney problems are given at the same time, especially certain antibiotics. Occasionally the kidney damage is severe enough to require the use of intravenous fluids or even an artificial kidney machine (hemodialysis). If your kidney function is poor prior to transplant, there is an increased risk that you may develop kidney failure requiring hemodialysis.

Destruction of red blood cells (hemolysis) often occurs while on CSP, and sometimes CSP needs to be withheld or discontinued for this reason. There is a risk of headaches and seizures while taking cyclosporine. Episodes of bleeding into the brain have occurred in two patients on similar protocols that may be related to CSP therapy. During treatment, CSP blood levels will be monitored periodically to determine if there is an increased risk of side effects that warrant adjusting the dose.

Central Venous Catheter. A central venous catheter is a hollow tube that is placed in a large vein inside the body. It is used to give intravenous medicine and to withdraw blood for lab tests. It is placed surgically, often using a local anesthetic (numbing medicine injected into the skin), and can cause some discomfort. There has been considerable experience with the use of central venous catheters. Complications have included clotting (accumulation of aggregates of blood cells that block the lumen of the catheter) and local infection, which sometimes causes an infection in the blood. Clotting may require that the catheter is removed or that you receive treatment of the clot with a fibrinolytic agent (Tissue Plasminogen Activator [t-PA] - a medicine that dissolves blood clots). Occasionally, there has been skin redness at the catheter exit site, which may require treatment with an antibiotic.

Bone marrow sampling: All patients will need to have marrow sampling performed. The risks of bone marrow sampling include slight pain, the possibility of infection, temporary bruising and bleeding around the site of the blood draw. There is a small additional risk of damage to the pelvis and nerve damage.

Risk to the Unborn: You should ***not*** become pregnant or father a child while on this study. The treatments in this study have 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 or men who have the potential of fathering a child must use some form of effective birth control for one year after transplant. Effective birth control would be defined as the following: 1) refraining from all acts of vaginal intercourse (ABSTINENCE); 2) consistent use of birth control pills; 3) injectable birth control methods (Depo-Provera); 4) tubal sterilization or male partner who has undergone a vasectomy; 5) placement of an IUD (intrauterine device); and, 6) use, with every act of intercourse, of a diaphragm with contraceptive jelly and/or condoms with contraceptive foam.

Sterility and Future Childbearing Potential for Men and Women: Chemotherapy and/or irradiation may affect fertility. Male patients may become sterile (unable to produce sperm). Female patients may find that their menstrual cycle becomes irregular or stops permanently. However, this DOES NOT MEAN THAT YOU CANNOT BECOME PREGNANT OR FATHER A CHILD, and you must use some effective method of birth control for at least one year after the transplant. Damage to ovaries and testes may result in birth defects or permanent inability to have a child or become pregnant. You should discuss these risks and options in detail with your doctor before entering this study.

- **Are there benefits to taking part in this study?**

The primary possible benefit is that it may provide an effective and potentially curative treatment for the patient's disease without the risks of treatment with high doses of radiation and chemotherapy. We cannot and do not guarantee the patient will benefit by taking part in this study. The treatment patients receive may even be harmful. Doctors feel that participation in this

study will give the patient at least as good a chance of surviving CLL as the patient might expect from other treatments. We hope the information learned from this study will benefit other patients with this type of leukemia in the future.

- **What if new information is learned while I am in this study that might affect my health?**

If we learn any important new information that might affect your health, welfare, safety, or willingness to stay in the research study, your doctor (attending physician) will tell you. You may be asked to sign another consent form if you wish to stay in the research study at that time.

- **What other treatment options are there?**

Instead of being in this study, you can decide to have:

- No treatment.
- A conventional allogeneic or autologous stem cell transplant, if eligible.
- Conventional chemotherapy, if appropriate.
- Biological (antibody) therapy, if appropriate.
- Experimental chemotherapy for patients with CLL who fail fludarabine, if eligible.

In general, patients who do not respond to treatment with fludarabine or who have cytogenetic abnormality of deletion 17, survive less than 12 months without treatment or with conventional chemotherapy. Nearly all patients who experience worsening of their CLL after prior fludarabine treatment fail to respond to further treatment with fludarabine or similar medicines. For some patients in this situation, antibody therapies can improve symptoms. For other patients, an autologous transplantation may get rid of CLL, but it may come back at a later date. For patients who are eligible, high-dose chemotherapy with or without radiation followed by receiving stem cell transplantation from another individual may get rid of CLL, but this procedure may have complications early after the transplant. Please talk with your doctor about these and other options before you enter the study. You may continue to discuss other options that may become available during the research study.

- **Can I change my mind about taking part in this study?**

Yes, you can change your mind. You have the right to choose whether or not you want to take part in this research study. You may decide to stop taking part in the study once you have started. Leaving the study will not result in any loss of benefits that you already have.

If you withdraw after some of the treatment is given but before you get the stem cells transplant, then you might experience some delay in regaining your full marrow function. This might require some additional supportive care and transfusion of blood products. However, we anticipate that the marrow function will eventually come back after this mild form of treatment.

It is <u>very</u> important to let your doctor (attending physician) know right away if you want to stop taking part in this study. Your doctor will talk with you about your choices.

➢ **How will information about me be kept private?**

We will try to keep your personal information as private as we can. There is no guarantee of absolute privacy. Your personal information may be disclosed if required by law. Organizations that are listed below may inspect or copy your research records for quality assurance and data analysis. Your research records will identify you by name and will include things such as your medical history, results of your blood tests and exams, reports from your surgery and treatment, reports of your office visits.

➢ **Who may see my research information?**

In order to evaluate the results of the study, individuals from the Fred Hutchinson Cancer Research Center (FHCRC) may need to review medical records that identify you by name. These individuals include investigators directly involved in the study, institutional committees responsible for reviewing the safety and progress of studies, and members of the Institutional Review Board (this Committee is responsible for protecting the rights of persons taking part in research). In order to evaluate the results of this study, individuals from the National Cancer Institute might also need to review medical records that identify you by name.

Your research records may be made available to the following organizations:

- The Fred Hutchinson Cancer Research Center (FHCRC)
- The University of Washington (UW)
- The Seattle Cancer Care Alliance (SCCA)
- National Institutes of Health (NIH)
- Office for Human Research Protections (OHRP)
- The Food and Drug Administration (FDA)
- Institutional Review Board (IRB)

Your identity will not be revealed in any publication or presentation of results. Study records will be maintained indefinitely for the purpose of analysis and follow-up.

➢ **What are the costs?**

You and/or your insurance company will pay all medical expenses relating to, or arising from, this study. You and/or your insurance company will be responsible for all procedures related for your treatment under this study. You and/or your insurance company will not be responsible for any exceptional research sampling or procedure that is not directly related or necessary for your treatment under this study. If you are injured or become ill from taking part in this study, emergency medical treatment is available but will be provided at the usual charge. The attending physician will authorize medical care. No funds have been set aside to pay you in the event of injury. You or your insurance company will be charged for continuing medical care and/or hospitalization. You will not be paid for taking part in this study. If you have questions regarding your costs, financial responsibilities, and/or medical insurance coverage for this activity, please contact the SCCA Patient Financial Services Department at (206) 288-1113.

➢ **Do I have to be part of the study?**

Your decision to participate in this study is voluntary. You may choose either to take part or not to take part in this research study. You may decide not to participate in this study at any time, for any reason, without notice. However, early discontinuation of the drugs that suppress (hold back)

the immune system, CSP and MMF, after stem cell transplant could lead to rejection of the donor stem cells or life threatening GVHD.

We request that you talk with the research physician and your regular doctor prior to withdrawing from the study. You will continue to receive medical care even if you decide to discontinue treatment on this study. If you have questions about the study, please talk with your physician or one of the investigators listed at the beginning of the consent. Do not sign this form unless you have had the chance to ask questions and have received satisfactory answers. You may also wish to discuss this matter with a relative or friend.

- **What are my rights as a study participant?**

Even after you agree to take part in this study, you may withdraw at any time. Before withdrawing, you should notify one of the people involved with this research. This will allow that person or someone else supervising the research to inform you of the medical risks associated with withdrawing. The medical risks may be substantial. You can choose to withdraw one of two ways. In the first, you can stop your study treatment, but still allow the study staff to follow your care. In the second, you can stop your study treatment and not have any further contact with the study staff. Either way, there will be no penalty or loss of benefits that you are already entitled to. Your decision will not affect your routine medical treatment, your relationship with those treating you, or your relationship with the study staff. If you withdraw from study therapy, you will still continue to receive medical care.

- **Who can I call if I have questions or problems?**

For Questions About	Please Contact
This study and what it involves	Your doctor (attending physician) or one of the investigators listed at the beginning of the consent
Your rights as a participant in a research study	Karen Hansen, in the Institutional Review Office, FHCRC at 206-667-4867
Your bills and health insurance coverage	Seattle Cancer Care Alliance, Patient Financial Services at 206-288-1113
Research use of your blood or tissue sample, or research files	Clinical Research Division, Data Management Office, FHCRC/Clinical Research Division at 206-667-4728
Research related injury	Your physician or one of the investigators listed at the beginning of this consent
Emergency care	**Emergency (24 hour) phone**: (206) 598-8902

➢**What about use of my tissue/blood cells for research?**
An Institutional Review Board (IRB) must also approve any future or new research study using your tissue. The IRB is a group of people who review research studies to protect your rights. The research that may be done with your tissue is not designed to specifically help you. It might help people who have cancer and other diseases in the future. Reports about research done with your tissue will not be given to you or your doctor. These reports will not be put in your health records. The research using your tissue will not affect your care.

Your tissue will be used only for research and will not be sold. The research done with your tissue may help to develop new products in the future, but you will not get paid.

The possible benefits of research from your tissue include learning more about what causes cancer and other diseases, how to prevent them and how to treat them. The greatest risk to you is the release of information from your health records. The chance that this information will be given to someone else is very small.

➢ **Where can I get more information about cancer and its treatment?**
You can call the Cancer Information Service at 1-800-4-CANCER or visit the National Cancer Institute's Clinical Trials Web Site at http://cancertrials.nci.nih.gov. You can also get information at any time from the doctor in charge of your medical care in this study or one of the study investigators.

CONSENT TO PARTICIPATE IN THE RESEARCH STUDY

I have carefully read this consent form. This study has been explained to me. I have a choice whether to take part or not to take part in this study. I have been told of the risks and benefits of taking part in this study. I have had the chance to ask questions about it, and all questions were answered to my satisfaction. I now agree to take part in this research study.

I also give permission to the people and organizations connected with this research study to review and copy my research records, both during the research and the long-term follow-up.

_____

Participant Printed Name, Signature, and Date

Legally Authorized Representative: If you have read this form (or had it read to you), asked any questions, and consent on behalf of the participant, please sign:

_____

Legally authorized representative / Printed Name, Signature, and Date

_____

Relation to the participant

MEDICAL STAFF PERSON'S STATEMENT

I have discussed the above research study, including the study purpose, procedures, risks and benefits, and possible alternatives, with the person signing above. All the elements of informed consent were reviewed and discussed with the subject. Special concerns that the participant expressed were noted and appropriately addressed. I encouraged questions and have answered all questions to the best of my ability. The participant is aware that he/she has a choice in taking part in this study. A signed copy of the consent form will be given to the participant.

_____ _____

Medical Staff Person's Signature Date

_____

Printed Name and Title of Medical Staff Person

_____

Signature of Any Additional Staff Person Present During Consent Process (if present)

1840.00A
Current Version: 12/25/2014
Previous Version: 4/8/2014
Copies to: Patient, Medical Records, Research File

Signed Consent MUST be sent to Data Management – LF-229
FHCRC, 1100 Fairview Ave N, Seattle, WA 98109-1024