IRO received 09/24/20

Fred Hutchinson Cancer Research Center
Seattle Cancer Care Alliance
University of Washington
Seattle Children's Hospital

Consent to take part in a research study: Randomized Feasibility Study of Discontinuation versus Continuation of Immunosuppressive therapy (IST) in Patients with chronic Graft versus Host Disease (cGVHD)

Patients stopping GVHD treatment

Principal Investigator: Stephanie Lee, MD, MPH
Fred Hutchinson Cancer Research Center
Telephone: 206-667-5160

Emergency number (24 hours):

Adult patients: (206) 598 - 5520
Ask to page: BMT fellow on-call

Pediatric patients: (206) 987- 4536
Ask to Page: Pediatric BMT fellow on-call

If you are serving as a legally authorized representative, a guardian, or are providing parental permission for a child in this study, the terms "participant", "you", and "your" refer to the person for whom you are providing consent or parental permission.

Important things to know about this study.

We are doing a research study to determine whether we can conduct a larger study to evaluate if continuation of immunosuppressive treatment (IST) prevents chronic graft-versus-host disease (GVHD) exacerbation, and to evaluate if there are factors that can help predict whether patients with chronic GVHD can successfully stop their IST.

If you agree to be in this study:

- You will be randomized to either standard taper and discontinuation of IST or to continue low dose IST (the dose that you are receiving now or a lower dose) for additional 9 months.

- We will follow you for 12 months after randomization with monthly evaluations, either at the Long-term follow-up (LTFU) clinic at the SCCA, at your local

oncologist's clinic, or with a phone or email contact by a member of the study team. At those evaluations we will assess your GVHD status and IST, as well as any other health problems you may have.

- After your active participation in the study we would like to review your medical chart to collect information about your health until the end of the study.

You do not have to join this study. You can choose to follow standard taper of IST instead of participating in this study. We will give you details about the purposes, procedures, risks and possible benefits related to this study. We will explain other choices that you have. We will also give you any other information that you need in order to make an informed decision about joining this study.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

We invite you to join this research study.

We invite you to join this research because you have chronic (GVHD) that is under control, and your physician has been considering discontinuing your immunosuppressive medications (IST) soon. Up to 40 patients will join this study.

Research is not the same as treatment or medical care. The purpose of a research study is to answer scientific questions.

You do not have to be in the study. You are free to say "yes" or "no", or to drop out after joining. If you say "no," you would have no penalty or loss of benefits. Whatever you decide, your regular medical care would not change.

Why are we doing this study?

We are doing this study to determine whether we can conduct a larger study to evaluate if continuation of IST prevents chronic GVHD exacerbation, and to evaluate if there are factors that can help predict whether patients with chronic GVHD can successfully stop their IST.

There are two groups of participants in this study. Patients on one group (standard of care arm) will follow standard taper and discontinuation of IST, while patients on the second group (investigational arm) will continue low dose of IST (the dose you are receiving now or a lower dose) for additional nine months prior to tapering the drug to off. This is how we hope to find out if continuation of IST decreases the risk of GVHD exacerbation.

If you join this study, you would not be allowed to choose the treatment. You would have a 1-in-2 chance of receiving longer duration of IST.

What research tests, procedures, and treatments are done in this study?

If you join this study, we would do these tests and procedures:

- We will ask that you donate blood samples for research. However, you can still be on the study even if you decide not to donate blood for research. Even if you agree to donate blood, you can change your mind at any time. For adult patients and pediatric patients who weigh > 40 kg, we would like to collect 40 mL (about 2.5 tablespoons) at the time of enrollment, randomization, and then monthly until one year after randomization. Additionally, we would like to collect blood if you restart or increase the dose of IST. Blood collection volumes will be weight-adjusted for children in accordance with the chart below:

	25-40 kg	10-24.99 kg	<10 kg
Maximum volume of each blood draw	20 mL	10 mL	5 mL
Maximum volume in 1 year	260 mL	130 mL	65 mL

  If you are unable to travel to the transplant clinic, the study team may provide your local doctor's office or laboratory with a collection kit. A study team member will contact you to coordinate local sample collection. Only laboratory staff or other authorized personnel can collect and send blood samples for this study. Please contact the study team if you have any questions or problems with the collection kits.

- We will ask adult participants to complete questionnaires up to 7 times during the study: when you join the study, when you are randomized to one of the two study arms, every three months after randomization, at the end of the study participation, and if your immunosuppression therapy restart or dose is increased. The questionnaire will be given to you in the clinic or may be mailed to you. The questionnaire has approximately 60 questions and will take about 10 minutes to answer. Some of the questions may be sensitive. Questions that make you feel uncomfortable would not have to be answered.

- Females of childbearing potential will be required to take a pregnancy test at enrollment.

- If you or your partner becomes pregnant while you are participating in this study, we will follow the pregnant female for pregnancy outcome.

- We will collect information about your health from your medical records. Results from your clinical laboratory tests will be collected as well.

How long would you stay in this study?

If you join this study, you would stay in the study for 12 months after randomization to one of the two study groups. During this time we will follow you with monthly evaluations, either at the Long-term follow-up (LTFU) clinic at the SCCA, at your local oncologist's clinic, or with a phone or email contact by a member of the study team. At those evaluations, we will assess your GVHD status and IST, as well as any other health problems you may have.

- After your active participation in the study we would like to review your medical chart to collect information about your health. We would like to keep track of your medical condition until the end of the study.

- Doctors could take you out of this study at any time. This would happen if:
  - They think it is in your best interest not to continue in the study.
  - You are not able or willing to follow study procedures.
  - The whole study is stopped.

If you withdraw from the study for any reason, previously collected information would remain in the study records and would be included in the analysis of results. This information could not be removed from the study records.

Long-term follow-up means keeping track of someone's medical condition for a long time. If you join this study, we would like to review your medical chart to collect information about your health, to see how you are doing. We would also ask your doctor to send a copy of your medical records. This information will help us learn about the long-term effects of longer continuation of IST.

You do not have to be in long-term follow-up. You could say "yes" or "no". Either way, you could still join this study. If you drop out of the study, you would be asked if we could call you or send you a survey once a year.

If you choose not to join long-term follow-up, you would not be contacted regularly, and we would not ask your doctor to send medical records, but we might still need to contact you for some other reason.

What are the side effects (risks)?

In this part of the consent form, we describe the side effects we expect from the tests and treatments in this study.

- Continuation of IST may increase the risks of infection, organ dysfunction and possibly relapse of cancer. As you have already received IST for treatment of your chronic GVHD, we do not know if participation in this study and being randomized to continue a low dose IST (the dose that you are receiving now or a lower dose) will increase these risks.

- Tapering off of your IST may increase the risk of return of chronic GVHD signs and symptoms, which would likely result in return to IST therapy to control the chronic GVHD. Resuming IST treatment may increase the risks of infection, organ dysfunction and possibly relapse of malignancy.

- The blood draw may briefly cause discomfort, bleeding, small blood clots, bruising, or swelling at the site of the needle stick. There is a small chance you may feel faint, lightheaded, or nauseated while your blood is being drawn. Care will be taken to avoid these risks.

- There is a slight risk of loss of confidentiality.

If you join this study, we would tell you if we discover new side effects that could affect you.

Non-physical risks

If you join this study, non-physical risks are:

- You might not be able to work.
- Results of genetic tests might be released by accident. This risk is very low, because we keep personal information private. If these results became known, you could have problems with family members or insurance.

What are the benefits?

We do not know if this study will help patients directly, however, prolonged administration of IST may decrease the risk of chronic GVHD exacerbations. If you take part in this study there may not be direct medical benefits to you, but you may benefit by being closely followed for your health status. We hope the information we learn from this study will help other people with chronic GVHD in the future.

You have other choices besides this study.

You do not have to join this study. You are free to say “yes” or “no”. Your regular medical care would not change if you decide to say “no”.

You have other choices for treatment, which may include other medications, treatments, or dose changes in your current medications. Each of these choices has risks and benefits. You should talk to your doctor or healthcare provider about these choices.

Protecting Privacy as an Individual and the Confidentiality of Personal Information

If you join this study, some people or organizations might need to look at your medical records and research records for quality assurance or data analysis. They include

- Researchers involved with this study.
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Research Center IRB. An IRB is a group that reviews the study to protect the rights and welfare of research participants.
- Fred Hutchinson Cancer Research Center, University of Washington, Seattle Children's, and Seattle Cancer Care Alliance.
- US National Institutes of Health, National Cancer Institute, Office for Human Research Protections, Food and Drug Administration, and other regulatory agencies as required.

We will do our best to keep personal information confidential. But we cannot guarantee total confidentiality. Personal information may be given out if required by law. For example, workplace safety rules may require health workers to contact you about lab tests. Or a court may order study information to be disclosed. Such cases are rare.

We will not use personal information in any reports about this study, such as journal articles or presentations at scientific meetings.

If you join this study, information about your participation would be made part of your permanent medical record. This information would include a copy of this consent form. If an insurance company or employer or anyone else were authorized to see your medical record, they would see a copy of this consent form.

How is my genetic information protected?

A federal law called the Genetic Information Nondiscrimination Act (GINA) helps protect genetic information about people who join research studies.

GINA restricts access to genetic information so that it cannot be used for health insurance coverage decisions. GINA prevent health insurance companies or group health plans from

- Asking for genetic information obtained in research studies, or
- Using genetic information when making decisions regarding your eligibility or premiums

GINA does not help or protect against genetic discrimination by companies that sell life, disability or long term care insurance.

Would we pay you if you join this study?

There is no payment for being in this study.

Would you have extra costs if you join this study?

If you join this study, you would have some extra costs. Your insurance company might pay these costs, but some insurance policies do not cover these costs. We could help find out whether your insurance company would cover these costs.

The extra costs are:

- Cost of tests that are given more often than usual.
- Cost of standard doctor visits and lab tests.

If you join this study, you or your insurance company would have to pay for the costs of standard treatment in this study.

What if you get sick or hurt after you join this study?

For a life threatening problem, call 911 right away or seek help immediately. Contact your study doctor when the medical emergency is over or as soon as you can.

For all other medical problems or illness related to this research, immediately contact the study team in person or call (206) 667-5854. They will treat you or refer you for treatment. You or your health insurance will have to pay for the treatment. There are no funds to pay you for a research-related injury, added medical costs, loss of a job, or other costs to you or your family. State or national law may give you rights to seek payment for some of these expenses. You do not waive any right to seek payment by signing this consent form.

You or your insurer will be billed for treatment of problems or complications that result from your condition or from standard clinical care.

You would not lose any legal right to seek payment for treatment if you sign this form.

What will my information and/or tissue samples be used for?

Your blood samples will be stored in a repository. Your samples may be used to study chronic GVHD or other transplant-related complications.

During this study, if the researchers learn new information that may be important to your general health or to your disease or condition, they will share that information with you. Only results of clinically approved tests that are directly related to your health will be shared with you. Results of research tests will not be shared with you or your doctor.

In addition, be aware that by agreeing to participate in this study, your information or blood samples could be used for future research studies or sent to other investigators for future research studies without additional consent from you. These future research studies will be reviewed by an oversight group known as an institutional review board if required by law. The information that identifies you will first be removed from your information or blood samples. If you do not want your information or blood samples to be used for future research studies without your consent, you should not participate in this study.

If you decide later that you do not want some or all of your samples to be used for research, you may contact Dr. Stephanie Lee at (206) 667-5160 and your samples will be destroyed if they have not already been analyzed for research.

Your samples contain DNA. DNA makes up the genes that serve as the "instruction book" for the cells in our bodies. By studying genes, researchers can learn more about diseases such as cancer. There are many different types of genetic tests. The testing on your blood samples might include genetic testing called whole genome sequencing. Whole genome sequencing looks at all the known genes in your cells.

This type of testing can provide useful information to researchers. It can also present risks if the test results became known to others, for example you could have problems with family members or insurance companies. There is also a risk that these test results could be combined with other genetic information to identify you.

Future genetic research

Several genetic databases are available to help researchers understand different diseases. These databases contain DNA code and medical information from participants who have various diseases.

As part of this study, we would like to release DNA code and information about your medical condition into a genetic database in order to help future research. The genetic database would not contain names, addresses, or other information that could be used to identify you.

The DNA code in a genetic database cannot be used by itself to identify any specific person. A researcher who already has DNA code about you could use information from a genetic database to learn more about you. Once we release information to a genetic database, we no longer have any control over the use of this information.

Your rights

- You do not have to join this study. You are free to say “yes” or “no”.
- If you get sick or hurt in this study, you do not lose any of your legal rights to seek payment by signing this form.

- During the study, we might learn new information that you need to know. For example, some information may affect your health or well-being. Other information might make you change your mind about being in this study. If we learn these kinds of information, we would tell you.
- If you join this study, you would not have to stay in it. You could stop at any time (even before you start). Your regular medical care would not change. You would have no penalty for stopping, but it would be better not to join the study if you think that you would change your mind later.
- Before you leave the study, the doctor might ask you to continue in the long-term follow-up part of the study.

Your responsibilities

If you join this study, you would have some responsibilities.

- Follow the schedule of study visits and procedures.
- Takes study medications as directed.
- Tell your doctor right away if you become or think you may have become pregnant or if you learn that you have or may have fathered a child.
- Tell us about side effects.

For more information

If you have questions or concerns about this study, you could talk to your doctor anytime. Other people you could talk to are listed below.

If you have questions about:	Call:
This study (including complaints and requests for information)	206-667-5160 (Dr. Stephanie Lee)
If you get sick or hurt in this study	206-667-5160 (Dr. Stephanie Lee)
Your rights as a research participant	206-667-5900 or email irodirector@fredhutch.org (Director of Institutional Review Office, Fred Hutchinson Cancer Research Center)
Your bills and health insurance coverage	206-606-1113 (Seattle Cancer Care Alliance Patient Financial Services)

Emergency numbers (24 hours):

Adult patients: (206) 598 - 5520
Ask to page: BMT fellow on-call

Pediatric patients: (206) 987- 4536
Ask to Page: Pediatric BMT fellow on-call

Read each question and think about your choice. When you decide on each question, please circle **YES** or **NO**.

Is it OK if someone contacts you in the future to ask you to donate more blood samples for research? (circle one)
YES **NO**

Is it OK if we send your genetic information to one or more databases for future research? (circle one)
YES **NO**

Signatures

Please sign below if you:

- have read this form (or had it read to you);
- had the opportunity to ask any questions you have;
- had the opportunity to discuss the research with the person obtaining consent; and
- agree to participate in this study.

Participant (age 14+):

Printed Name	Signature	Date

Parent or legal guardian:

Printed Name	Signature	Date

Researcher's statement

I have discussed the research study, including procedures and risks, with the person signing above. A copy of the signed consent form will be given to the participant.

Person obtaining consent signature:

Printed Name	Signature	Date