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Fred Hutchinson Cancer Center
University of Washington School of Medicine

Consent to take part in a research study:

Phase 2 pilot study to evaluate efficacy and safety of anakinra to prevent CD19-targeted CAR-T cell-related cytokine release syndrome (CRS) and neurotoxicity in patients with B cell lymphoma

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Emergency number (24 hours): 206-598-8902

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.

You are invited to participate in a research study. The purpose of this research is to find out if anakinra (a drug that blocks a protein involved in inflammatory processes in the body) can help in preventing development of cytokine release syndrome (CRS) and neurotoxicity, which are common side effects of treatment with chimeric antigen receptor (CAR) T cells.

The study is conducted by Fred Hutch researchers, who are the regulatory sponsor of the study (Sponsor). Sobi, Inc, a biopharmaceutical company, provides the study drug, anakinra, and financial support for this study, but is not the regulatory sponsor of the study.

If you agree to join the study, you will receive anakinra for 14 days, starting on the day of your CAR-T cell infusion.

We do not know if anakinra will help to prevent CRS or neurotoxicity. Anakinra could cause side effects.

You do not have to join this study. You could choose not to participate in the study and just receive standard methods to treat CRS and neurotoxicity if you develop these complications after CAR-T cell infusion.

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. Afterwards, you can ask questions that will help you decide whether to join the study. If you join this study, we would 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 study because you have B cell non-Hodgkin lymphoma (B-NHL) that has either recurred or not responded to conventional chemotherapy or other treatments and you are about to get treatment with lisocabtagene maraleucel (liso-cel; Breyanzi), a CAR-T cell therapy. You will be able to participate in this study even if you receive treatment with a non-conforming (out-of-specification) liso-cel product.

Research is not the same as treatment or medical care. The purpose of a research study is to answer scientific questions. We will enroll up to 25 people with B-NHL for this research study.

You do not have to be in this study. You are free to say yes or no, or to drop out after joining. There is no penalty or loss of benefits if you say no. Whatever you decide, your regular medical care will not change.

Why are we doing this study?

We are doing this study to see if a drug called anakinra can decrease the risk of developing CRS and neurotoxicity, which are common complications of CAR-T cell therapy. Anakinra is a drug mimicking a natural protein that blocks the interleukin-1 receptor (IL1-R). IL-1 is a protein involved in inflammatory processes in the body and animal models have shown that anakinra may help in preventing CRS and neurotoxicity after treatment with CAR-T cells.

Anakinra is approved by the U.S. Food and Drug Administration (FDA) for use in other health conditions, but its use for prevention of CRS and neurotoxicity related to CAR-T cells is experimental.

In this study, we want to learn if administration of anakinra before and for two weeks after infusion of CAR-T cells may prevent or decrease the severity of CRS and neurotoxicity.

We will treat up to 10 patients.

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

If you decide to join this study, we will do the following research tests and procedures, which are performed in addition to your usual care. Where possible we will try to schedule the times and locations of research tests at the same time as the tests done as part of your usual care.

To determine if you are eligible for this study, a number of routine tests will be evaluated. This will include routine blood tests, including testing for blood grouping, viruses like hepatitis and HIV, complete blood counts, pregnancy test (if applicable) and metabolic function panels. You will have medical tests done to evaluate your heart, lungs and other organs (if necessary).

There are several parts to this study.

- **Anakinra administration.** Anakinra at a dose of 200 mg will be given intravenously as one injection over 10 minutes once daily (approximately every 24 hours) for 14 days, to start on the day of liso-cel infusion (day 0 through day 13). The first dose will be administered approximately 2-4 hours before the liso-cel infusion. If you develop side effects related to your CAR-T cell treatment, the dose of anakinra may be increased.
- **Blood tests.** We would like to obtain up to approximately 10mL (2 teaspoons) of blood to measure anakinra levels at the following timepoints:
    - Approximately 4 hours after the first anakinra administration
    - Approximately 24 hours after the first anakinra administration and immediately prior to the second anakinra administration

  The schedule may vary depending on your clinic schedule, logistics and your medical condition. If your schedule is modified, samples may be recollected.

If sampling of tissues or fluids (e.g., bone marrow, cerebrospinal fluid, pleural fluid, ascites, skin) is done as part of your clinical care, an additional sample may be obtained during the same procedure and sent to the FHCC for research studies.

If you consent to participate in the partner protocol FHCC 8682 "Collection of Samples and Data from Patients Undergoing Treatment with Commercial Chimeric Antigen Receptor Engineered T Cells", additional research samples may be obtained. Protocol FHCC 8682 will be presented to you separately.

How long would you stay in this study?

You will be actively participating in the study for approximately a month from the day of the first dose of anakinra. We will also follow the results of restaging that will be performed by your treating oncologist.

The study doctor or your doctor may take you out of this study at any time, whether you want to leave the study or not. This would happen if:

- They think it is not in your best interest to continue in the study.
- You are not able or willing to follow study procedures.
- The whole study is stopped.

If you are thinking about dropping out of this study, please tell the study doctor. The doctor can tell you about the effects of stopping. You and the doctor can talk about what follow-up care and testing would help you the most.

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.

What are the side effects (risks)?

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

With any new treatment or combination of treatments, there may be side effects that we do not know about and cannot predict. Although the study goal is to lessen side effects from CAR-T cells, we do not know if combination with anakinra will have that effect. Combining anakinra with CAR-T could worsen side effects of either or have other effects that we do not know about. In experiments in animal models, anakinra did not affect how well CAR-T cells worked against lymphoma and leukemia cells, but we do not know if anakinra will affect how well CAR-T cells work in humans, and it may decrease how effective the CAR-T cells are against the lymphoma cells.

If we learn about other side effects, we will tell you. We carefully watch everyone in the study for side effects. If you want more information about side effects and risks, ask the doctor or nurse.

You should talk to your doctor about any side effects that you have while you are in this study.

If they occur, side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects

Risks of anakinra

More likely side effects (>10%):

- Headache
- Vomiting
- Infections (generally mild), including skin infection, Upper respiratory tract infection (cold), pneumonia, and bone and joint infections)
- Infusion reaction (may include fever, chills, rash, itching, shortness of breath, low blood pressure or nausea)
- Joint pain
- Fever

Less likely side effects (1% to 10%):

- Nausea
- Diarrhea
- Decreased white blood cell count
- Decrease or increase in platelet count
- Rare side effects (<1%)
- Hepatitis (noninfectious)
- Hypersensitivity reaction (including anaphylaxis, angioedema, pruritus, skin rash, urticaria)
- cancer

Side effects of unknown frequency:

- Skin rash
- High cholesterol level

Risks of study procedures

Where possible, we will schedule study blood tests to take place at the same times as your regular clinical tests to minimize any risks and discomfort. If you have the tests done separately, the extra risks are as follows.

Blood tests

The risks of blood tests depend on whether the blood is taken by needle directly from a vein or from a device, such as a Port or Hickman catheter, that stays in place for blood tests. If blood is taken from a Hickman catheter, there is usually no pain or bruising.

Likely side effects (≥ 20%) of blood tests are:

- Temporary discomfort if blood is taken straight from a vein.
- A small bruise or redness at the site from which the blood was taken.

Less likely side effects (3-20%) of blood tests are:

- Fainting, sweating, or feeling sick in the stomach that gets better when you lie down and rest.
- Bruising larger than a "quarter" coin.

Rare but serious side effects (< 3%) of blood tests are:

- Infection from the blood draw.
- Injury to blood vessels, nerves, or other structures near the blood draw site.

Reproductive risks

Anakinra may involve unknown risks to an embryo, fetus (unborn baby) or nursing infant. Therefore, you could not join this study if you are pregnant, if you are planning to become pregnant, or if you are breast-feeding.

If you join this study, you would have to use an effective method of birth control from the time this form is signed until at least 4 months after the last dose of anakinra. If you are already using a method of birth control, you would have to check with the study doctor or a member of the study staff to make sure it is acceptable.

If you became pregnant after joining this study, you would have to notify the study doctor immediately. Participation in this study would end, and you would receive counseling and follow-up throughout the pregnancy and for about 6 months after the child is born.

The effects of anakinra on fathering a child are also unknown. Men who join this study must also agree to use one or more forms of effective and acceptable birth control from the time this form is signed until at least 4 months after the last dose of anakinra.

What are the benefits?

We hope this study will help participants by decreasing the risk of CRS and neurotoxicity after treatment with CAR-T cells, but we do not know if it will. Using anakinra to prevent CSR and neurotoxicity is experimental, and we are testing it. We hope the information from this study will help us find out if anakinra can help patients who receive CAR-T cells in the future.

If you join this study and develop CRS or neurotoxicity you will receive additional treatment as clinically indicated (for example: Tocilizumab and corticosteroids).

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 say "no".

If you do not join this study, you have other choices for treatment. Each of these choices has risks and benefits. Talk to your doctor about your choices.

Your other choices may include:

- Treatment of CRS and neurotoxicity if developed after CAR-T cell therapy, as clinically indicated (for example: Tocilizumab and corticosteroids).
- Supportive care
- A different research study
- Enrollment in this study may exclude you from other research studies.

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.
- The study Sponsor and their agents.
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Center IRB. An IRB is a group that reviews the study to protect your rights as a research participant.
- Fred Hutchinson Cancer Center and University of Washington,
- Office for Human Research Protections, Food and Drug Administration, and other agencies as legally required.
- Sobi, Inc, a biopharmaceutical company providing the study drug, anakinra, and financial support for this study.

We will do our best to keep your personal information confidential. But we cannot guarantee total confidentiality. Your 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 your personal information in any reports about this study, such as journal articles or presentations at scientific meetings.

Policies of the University of Washington (UW Medicine) and the Fred Hutchinson Cancer Center require that certain information about participation in this research must be included in permanent medical records.

If you join this study but do not already have a medical record at UW Medicine or FHCC, we would create a record even if the only connection with UW Medicine or FHCC involves this research study.

The information in the permanent medical record would include:

- Name of the study.
- Name of the group or company that is paying for the research.
- The number the group or company assigned to this study.
- The name of the researcher.
- The name of the study coordinator.
- Contact phone number for the study.
- Contact email address for the study.
- Emergency phone number for the study.
- A copy of this consent form.

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 you authorize others 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. You or your insurer will have to pay for the routine costs of treating your cancer in this study. Check with your insurer before you join this study as some insurers will not pay for research. Taking part in the study may lead to extra costs for you or

your insurance company because of the possibility of additional hospitalizations, procedures and blood tests.

The anakinra you receive during this study will be provided to you at no cost by Sobi Inc.

If you have any questions concerning your costs, financial responsibilities, and or medical insurance coverage for this activity, please ask your physician or contact the FHCC Patient Financial Services Department at (206) 606-6226.

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 Immunotherapy clinic by calling (206) 606-6000. They will treat you or refer you for treatment. If you are injured as a direct result of a defect in the manufacture of the study drug (anakinra) Sobi, Inc. may cover the costs for treatment of the injury. You or your health insurance will have to pay for the treatment of all other injuries. There are no other 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 blood samples be used for?

Your information and blood samples will be used for the purposes of this study.

Your blood samples might help researchers develop new products. This research could be done by for-profit companies. There is no plan to share with you any revenue generated from products developed using your blood samples.

During this study, if the researchers learn new information that may be important to your treatment, they will share that information with you.

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 tissue samples. If you do not want your information or tissue samples to be used for future research studies without your consent, you should not participate in this study.

Your anonymized study data and anonymized study samples may be shared with research collaborators which may involve data being transferred outside the US and to commercial partners for the purposes of research.

We invite you to donate blood samples for other research.

After we do tests on blood samples in this study, some samples may be left over. We invite you to donate this leftover blood for future research. This may include genetic research.

If you join this study, you would not have to donate tissue for future research. You would be free to say "yes" or "no." Regular medical care would not change if you say "no."

If you donate blood, it would be stored in a secure location. If we want to use your tissue for other research or share it with other scientists for research, an ethics review committee (IRB) would review the request. The IRB would decide if we need to ask you for permission to do the research.

Your donated blood would be used only for research. This research could be done by for-profit companies. Researchers would not report their results to you or your doctors. The research results would not be included in medical records. The results would not affect your medical care.

Research with tissue might help develop new products. If these products make money, there is no plan to share the money with the participants who donate the tissue.

If you donate tissue for research, you could withdraw the donation at any time by calling Dr. Gauthier at 206-667-2713. You would have no penalty for withdrawing the donation, and regular medical care would not change. We could not return donated samples, but we might be able to destroy the donated samples. We could not destroy samples if it is stored or shared without any label saying who donated it. In this case, it could still be used for research.

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.

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

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.
- Prevent pregnancy.
- 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)	206-667-2713 (Jordan Gauthier, MD; study PI)
If you get sick or hurt in this study	206-606-6000 (IMTX clinic)
Your rights as a research participant	206-667-5900 or email irodirector@fredhutch.org (Director of Institutional Review Office, Fred Hutchinson Cancer Center)
Your bills and health insurance coverage	206-606-6226 (FHCC Patient Financial Services)

Emergency number (24 hours): 206-598-8902

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

Do you agree to donate your tissue to study cancer? (circle one) **YES** **NO**

Do you agree to donate your tissue to study other health problems, such as diabetes, Alzheimer's disease, or heart disease? (circle one) **YES** **NO**

Is it OK if someone contacts you in the future to ask you to donate more tissue 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:

Printed Name	Signature	Date

Witness:

If you served as a witness during the consent process, sign below to indicate you attest to the accuracy of the presentation to the participant and the apparent understanding of the research by the participant.

Printed Name	Signature	Date

Interpreter:
If you served as an interpreter during the consent process, sign below to indicate you attest to the accuracy of the presentation to the participant and the apparent understanding of the research by the participant.

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

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