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Fred Hutchinson Cancer Center
University of Washington School of Medicine

Adult participant consent to take part in a research study

Rabies Vaccination to Assess Vaccine Responsiveness after B Cell Targeted CAR-T Cell Therapies

Short Title: **The RAV-CAR Study**

Principal Investigator:
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Emergency number (24 hours): 206-598-6190

Call the Fred Hutchinson Cancer Center Clinic at 206-606-7400, Monday through Friday, from 9:00 AM to 5:00 PM. At all other times, call the Paging Operator at the University of Washington Medical Center at 206-598-6190 and ask for the Infectious Disease Fellow on call.

If you are serving as a legally authorized representative, the terms "participant", "you", and "your" refer to the person for whom you are providing consent.

Important Things to Know About the Study.
You are invited to participate in a research study. The purpose of the study is to better understand the immune system after receiving CAR-T cell therapy. After your CAR-T cell therapy, it will take some time for your immune system to recover. This makes it more likely for you to develop an infection. We are conducting a study using the rabies vaccine to assess how your body responds to vaccines. Our bodies produce antibodies when they sense foreign cells. We will study the antibodies that are produced after each rabies vaccination to help us better understand whether your immune system will be able to respond to standard vaccinations after CAR-T cell therapy.

The Imovax Rabies Vaccine is an FDA approved vaccine that is usually used to protect patients from getting a rabies infection. This is an inactivated vaccine, so there is no risk of getting rabies infection from the vaccine. It is safe and approved for use in patients with cancer or other conditions that lower their immune system.

People who agree to join the study will be asked to join one of two groups. The first will receive standard vaccine doses in the upper arm muscles and attend up to 9 visits over approximately 6 months, although only 2 visits are needed in-person. The study will involve two vaccinations, primary and secondary, scheduled 6-10 weeks apart and up to 9 blood draws. The second cohort will receive their first dose split into 6 separate visits containing a partial dose over 17 days, with approximately two visits per week. The dose of each subsequent partial vaccine dose will increase, but the total amount of vaccine given will be the same as a standard single dose. At each of these 6 visits you will get a shot in the upper arm muscles. There will be a secondary vaccination scheduled about 6-10 weeks after the last dose of the initial vaccination series, and up to 10 blood draws in total. There will be up to 14 visits over approximately 6 months, although only 7 visits are needed in person.

You do not have to join this study. We will give you details about the purpose, 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.

The 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, you will sign this form and we will give you a copy of the form to keep for future reference.

We invite you to join this research study.
You are being asked to participate because you have had CAR-T cell therapy. Up to 43 people will participate in this study.

Research is not the same as treatment or medical care. The purpose of the 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.

What research tests, procedures, and treatments are done in this study?
If you agree to participate in the study, you will be asked to come to Fred Hutchinson Campus for blood draws and vaccine administration. If you are a part of the standard "bolus" dose cohort, you will be receiving two vaccinations 6-10 weeks apart. If you are a part of the fractional dose cohort, you will be receiving six partial doses over three weeks for your first vaccination and a final dose 6-10 weeks following the last partial dose for your second vaccination. Prior to the initial visit, the study team will review your medical records for information related to your CAR-T cell therapy. At the initial visit, there will be a blood draw (40 ml, up to 8 teaspoons) 15 minutes prior to the vaccination. The vaccine will be given in your upper arm muscle. We will ask you to stay 15 minutes after the vaccination for observation. After this initial visit, if you are in the bolus dose cohort you will be asked to provide additional blood at one, two, and four weeks post-vaccination. Similarly, if you are in the fractional dose cohort, you will be asked to provide additional blood at one, two, and four weeks after the final dose of the fractional dose series. These additional blood samples will allow us to measure the amount and type of antibodies that your immune system has made in response to the vaccine.

The second vaccination will be scheduled 6-10 weeks after the first vaccination or the final fractional dose of the first vaccination. There will be one blood draw prior to the second vaccination (40 ml, up to 8 teaspoons), and we will still ask you to stay for 15 minutes post-vaccination for observation. The follow-up schedule for the second vaccination will be the same as for the initial visit, with blood draws at one, two, and four weeks post-vaccination. There will be a final blood draw approximately 6 months after the initial vaccination for both cohorts.

If you prefer, you will have the option to self-collect the blood at home for the one, two, and four weeks blood draws after each vaccination for the standard dose cohort and the fractional dose cohort. This would reduce your in-person study visits to only the 2 or 7 vaccination timepoints (depending on the cohort). If you choose this option, we will provide you with a device called TASSO+ that will allow you to self-collect a small volume of blood (<1 teaspoon) using a disposable, sterile, needle-free device and mail the blood sample back to the study team. You will be asked to watch an instructional video on how to collect the sample at home. The study staff will then explain how to collect the blood using the device during a video or phone call. We may contact you to provide an additional sample if you did not collect enough

blood or there are issues related to the mail carrier service. The device will be provided to you by the study. Any unused TASSO+ devices will be returned at the end of the study.

After each vaccination, we will ask you to contact the study team if you feel you have had a reaction to the vaccine. There is a chance you may not be given the second vaccination or subsequent fractional doses of the vaccine. This might occur if something changes in your medical condition between your first and second vaccines. Another reason you might not get the second vaccination is if you have a serious reaction to the first vaccination.

What are the side effects (risks)?
You may experience pain, swelling or itching at the vaccine injection site. People who receive the rabies vaccine report the following symptoms:

Common Side Effects (more than 20% of patients)
- Headache
- Pain at injection site
- Myalgia (muscle pain)

Uncommon Side Effects (20% of patients or less)
- Dizziness
- Lymphadenopathy (swelling of the lymph nodes)
- Malaise (general sense of feeling unwell)
- Abdominal pain
- Nausea/vomiting
- Fever
- Headache
- Feeling lightheaded

Rare but potentially serious side effects that have been reported but are not definitively linked to the vaccine and are usually reversible
- Temporary loss of the ability to move or feel part of the body
- Visual disturbance
- Inflammation of the brain
- Anaphylaxis (an allergic reaction).

These side effects are common for many vaccines. How common these side effects are is known using standard dose approaches (“bolus”). This is the first time the rabies vaccine will be given in a fractional escalating dose, so we do not know if this will change the side effects of the vaccine. Understanding if fractional dosing changes the side effects of the vaccine is one of the goals of the study. We do know that in one other study using an experimental vaccine, the side effects were very similar using either standard “bolus” dosing or fractional dosing.

This product contains albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases and variant Creutzfeldt-Jakob disease. There is a theoretical risk for transmission of Creutzfeldt-Jakob disease but if that risk exists, the risk of transmission is considered extremely remote. No reports of transmission of viral diseases have ever been reported. However, as with any drug, there may be unanticipated side effects, and you should report any concerns to your study team. If you have a serious or concerning side effect after the first vaccination, your study team will discuss with you whether you want to proceed with a second vaccination.

Blood collection may cause brief pain and may cause dizziness. A bruise may form or there may be bleeding where the needle is inserted.

For self-collection of blood samples using the provided device, this may cause minor pain and bruising and may lead in rare cases to an infection where it is applied. This procedure is similar to using a finger prick and the risks are similar to getting blood for measuring your blood sugar. It has been used in thousands of people and no severe complications have been reported.

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

What are the benefits?
Because you will not receive the standard rabies vaccine schedule as part of this study, you will not be considered to be fully vaccinated against rabies in the event of a possible future exposure. In participating in the study, you will help us better understand if vaccination after CAR-T cell therapy can help prevent infections. If you would like, we will provide your clinical care team with aggregate results of the tests we perform from participants in this study. This may help them make decisions about your clinical care.

You have other choices besides this study.
You do not have to participate in this study. You may also withdraw from the study at any time.

Protecting Privacy as an Individual and the Confidentiality of Personal Information
To protect your identity and ensure privacy, your name and other identifying information will not be attached to records or samples released for research purposes. The study staff will assign a confidential code to your research records. Only the study doctor and authorized personnel will be able to connect this code to your name. 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. 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 any insurance company, employer, or anyone else authorized to see your medical record were to view it, they would see a copy of this consent form. Tasso Inc, the maker of the home collection device, will ship the device directly to you and will have access to your name and mailing address.

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

- The Fred Hutchinson Cancer Center (Fred Hutch)
- U.S. Office for Human Research Protections (OHRP)
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Center IRB. An IRB is a group that reviews the study to protect the rights and welfare of research patients
- Food and Drug Administration (FDA)
- Centers for Disease Control and Prevention (CDC)

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

This research is covered by a Certificate of Confidentiality from the U.S. government. This Certificate helps protect the confidentiality of information about people who join this study. If you join the study, the Certificate means that generally we would not have to give out identifying information about you even if we were asked to by a court of law. We would use the Certificate to resist any demands for identifying information.
We could not use the Certificate to withhold research information if you give written consent to give it to an insurer, employer, or other person.
This protection has some limits. We would voluntarily provide the information:

- To a member of the federal government who needs it in order to audit or evaluate the research.
- To the funding agency and groups involved in the research, if they need the information to make sure the research is being done correctly.
- To the federal Food and Drug Administration (FDA), if required by the FDA.
- To someone who is accused of a crime, if he or she believes that our research records could be used for defense.
- To authorities, if we learn of child abuse, elder abuse, or if participants might harm themselves or others.

Would you have extra costs if you join this study?
You will not be required to pay any money for participating in the study. You will not pay for any tests, procedures, or vaccinations directly related to the study.

Would we pay you if you join this study?
We will compensate you for participating in the study. You will receive up to $270 in gift cards for study participation. You will receive $100 at each vaccination visit and will receive an additional $70 after you complete the 6 months follow-up visit. If you decide to withdraw from the study prior to the end of the study, you will receive $10 for each blood sample completed.

1st Vaccination or completion of fractionated doses	2nd Vaccination (6-10 weeks after initial visit or final fractionated dose)	End of Study (6 months after initial vaccination)	Total Compensation
$100	$100	$70	$270

In addition, you will be reimbursed to cover the costs of travel. If an overnight stay is required, you will be reimbursed for lodging, meals, and incidentals.

What if you get sick or hurt after you join the 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, contact the study doctor listed on the first page. 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 of care.

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

What will my information and/or samples be used for?
Your information and samples will be used for the purposes of this study.

Your 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 tissue samples.

During this study, if the researchers learn new information that may be important to your general health or to your disease, with your permission, they will share that information with your clinical care team.

In addition, be aware that by agreeing to participate in this study, your information or tissue 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 samples. If you do not want your information or samples to be used for future research studies without your consent, please initial next to the appropriate option.

We invite you to donate your leftover samples for other research.
After we do tests on your samples, there may be some leftover. We invite you to donate this left over sample for future research.

If you join this study, you would not have to donate your samples for future research. You are free to say 'yes' or 'no'. Regular medical care would not change if you say 'no'.

If you donate your samples, it would be stored in a secure location. If we want to use your samples for other research or share it with other researchers, 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 samples would be used only for research. Researchers would not report their results to you or your doctors. The samples might be used by for-profit companies. If new products are developed and these products make money, there is no plan to share the money with participants who donate the samples.

If you donate your samples for research, you can withdraw the donation at anytime by calling, Dr. Hill at (206)667-6504. There is no penalty for withdrawing the donation, and regular medical care would not change. We will not be able to return the samples, but we might be able to destroy them. We will not be able to destroy any samples that have already been used.

Your rights
- You do not have to join this study. You are free to say yes or no. Your regular medical care will not change.
- If you join this study, you do not have to stay in it. You may stop at any time (even before you start). There is no penalty for stopping. Your regular medical care will not change.
- 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.

For more information
If you have questions or concerns about this study, you may talk to your doctor anytime. Other people you can talk to are listed below.

If you have questions about:	Please Contact
This study (including complaints and requests for information)	Dr. Joshua Hill 206-667-6504
If you get sick or hurt in this study	Dr. Joshua Hill 206-667-6504
Your rights as a research participant	irodirector@fredhutch.org or 206-667-5900 (Director of Institutional Review Office, Fred Hutchinson Cancer Center)
Your bills and health insurance coverage	The financial services department at the medical center where you will be treated.

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Signatures

Earlier in the consent form, we told you about the possibility of donating your left over samples. Please **INITIAL** in the box next to the **ONE** option you choose.

_____ I agree to allow my leftover samples and information to be used for other studies.

Or

_____ I do not agree to allow my extra samples and information to be used in other studies.

If you have read this form (or it was read to you), you have asked any questions you may have, and you agree to participate, please sign below:

Participant (18+ years old): Printed Name	Signature	Date

If you served as an interpreter or witness during the consent process, sign below to attest that the contents of this consent form were presented accurately to the participant; and that it is apparent to you that the participant understands the research study they are joining:

Witness or Interpreter: 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.

Printed name of Researcher	Signature	Date

Protocol: 10411
Current version date: 07/12/2023
Previous version date: 04/19/2023
Copies to: Participant, medical file, research file.

Signed consent MUST be sent to Data Management-LF-229
Fred Hutch, 1100 Fairview Ave N, Seattle, WA 98109-1024