COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH STUDY

YALE UNIVERSITY

Study Title: Evaluating the Immune Response to COVID-19 Vaccination in B-cell Depleted Patients
Sham Vaccine Group
Principal Investigator (the person who is responsible for this research): *Erin Longbrake, MD, PhD*
Phone Number: 203-287-6100

Research Study Summary:

- We are asking you to join a research study.
- The purpose of this research study is to study how individuals on certain immune-modifying medications respond to vaccination against COVID-19.
- Study procedures will include: sham vaccination with saline, clinical data collection, one skin biopsy procedure.
- Two visits are required.
- Each visit will take approximately 15-20 minutes. There are some risks from participating in this study. Skin biopsies may cause some discomfort, bleeding or bruising at the site. Any time a biopsy is performed a scar will result. The size of the scar is usually the size of the biopsy (about 3 mm) or smaller.
- The study may have no benefits to you. You will not receive any direct benefits from this study. We hope that the information we learn in this study will help us understand better how people taking immune medications (e.g. rituximab or ocrelizumab) respond to vaccination against COVID-19. This information will help physicians and patients make decisions about the frequency and timing of vaccinations in the future.
- There are other choices available to you outside of this research. You can choose not to participate. Choosing not to participate will not cause any penalty or loss of benefits to which you are otherwise entitled (such as your health care outside the study, the payment for your healthcare or your healthcare benefits).
- Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You can also change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.
- If you are interested in learning more about the study, please continue reading, or have someone read to you, the rest of this document. Take as much time as you need before you make your decision. Ask the study staff questions about anything you do not understand. Once you understand the study, we will ask you if you wish to participate; if so, you will have to sign this form.

Why is this study being offered to me?
We are asking you to take part in a research study because you are a healthy individual or because you have MS. We are looking for up to 20 participants who would be willing to have a sham vaccine (saline) followed by skin biopsy. You would not have any additional study requirements.

Who is paying for the study?

This study is paid for directly or indirectly by:
- Yale University Department of Neurology
- Government grants (e.g. National Institute of Health)
- Foundation grants

What is the study about?
The purpose of this study is to better understand how individuals taking B-cell depleting medications for autoimmune diseases will respond to COVID-19 vaccination compared to those who are not taking these medications. Right now, the safety and effectiveness of the vaccine has not been specifically studied in patients taking immune medications.

People who have a sham vaccination will serve as controls for people participating in the main study. Having a control is needed to know what changes are caused by the active vaccination versus by just having an injection in their skin.

What are you asking me to do and how long will it take?
If you agree to take part in this study, this is what will happen: You will have a sham vaccination. This means that a small needle will be used to inject a small amount of saline (an inactive agent) into your arm. The size of the needle and the volume of fluid injected would match those that are used for COVID vaccines. Approximately 4 days later, you will have a skin biopsy visit. Each visit could take up to 15-20 minutes.

Clinical Information: The research team will access your medical record and extract information about you and your health. They may look at the following types of information:
- Name, birthdate and medical record number (used for screening purposes)
- Demographics
- Information about your medical history, lab results, MRI images and results, and medications
- Information about your health status and quality of life
- Contact information, so that we can reach you for follow-up

Skin Biopsies: Each skin biopsy procedure consists of two biopsies. One skin biopsy will be taken from your vaccinated arm, close to the area where you got your sham vaccine. A second biopsy will be taken from the same location on your other arm. Prior to skin biopsy, the skin will be numbed with medications called lidocaine and epinephrine. This is the medication used by dentists when filling cavities. The numbing stings for about 30 seconds. Once the skin is numbed, a dermatologist will remove a small piece. Each skin biopsy will be about 3 mm (the size of a pencil eraser).

What are the risks and discomforts of participating?

Clinical Information: There are no physical risks to you for allowing your clinical information to be used in future research studies. In the unlikely chance that your information is viewed by someone outside the research team, there is a risk of breach of confidentiality (see section below on “How will you keep my data safe and private”).

Before being used for research purposes or shared with any collaborating group, your data will be stripped of personal identifiers and information that can link the data to you (“de-identified”). Your de-identified data may be deposited into larger, national databases when required by federal funding agencies.

Genetic information: There is a risk that your information could be misused. The chance of this happening is very small, and we have protections in place to lower this risk. There can be a risk in uncovering genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a research study. There is a federal law called the Genetic Information Nondiscrimination Act (GINA) that makes it illegal for health insurance companies, group health plans and most employers to use genetic information against you. This law generally will protect you in the following ways:

• Health insurance companies and group health plans may not request your genetic information that we get from this research.
• Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
• Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

This Act does not protect you from discrimination by companies that sell life, disability or long-term care insurance. At this time, the chances that we would be required to share any of your genetic information with companies like this are small. No genetic information will be reported back to you or recorded in your medical record as part of this research study.

Sham vaccine: You may notice minor soreness or a tiny amount of bleeding at the site of the sham vaccine.

Skin biopsy: There may be some discomfort, bleeding or bruising at the site. There is a small risk of infection. Any time a biopsy is performed, a scar will result. The size of the scar is usually the size of the biopsy, or slightly smaller, since most scars contracts. Very rarely a raised scar called keloid can form. There is also a small likelihood of local bleeding at the site of biopsy at a later time before biopsy heals. Having a dermatology-trained physician perform skin biopsy minimizes these risks. In addition, there is an exceedingly rare chance of allergy to the topical and/or injected anesthetic used for skin biopsy. There is also a chance of fainting.

Participating in the sham vaccine study will delay receiving active vaccine for 3-5 days. Please consider receiving active vaccine after your participation in the study is complete, if this is recommended for you under the current CDC guidelines. Your medical team can advise you about whether this is recommended for you.

How will I know about new risks or important information about the study?

There may be risks that are currently unforeseeable. We will tell you if we learn any new information that could change your mind about taking part in this study.

How can the study possibly benefit me?

The study may have no direct benefits to you. You will not receive any direct benefits from this study. We hope that the information we learn in this study will help us understand better how people with autoimmune diseases taking immune medications (e.g. rituximab or ocrelizumab) respond to vaccination against COVID-19. Results from people who have sham vaccinations and skin biopsies are needed to understand the results we get from people who had a COVID vaccine. This information will help physicians and patients make decisions about the frequency and timing of vaccinations in the future.

Are there any costs to participation?

You will not have to pay for taking part in this study. The only costs include transportation and your time coming to the study visits.

Will I be paid for participation?

You will be paid $100 after sham vaccination and skin biopsy.

We will use a Bank of America pre-paid debit card to provide the payment for taking part in the study unless specific arrangements are made for an alternate method of payment. We will have to share your name, address, and telephone number with Bank of America for ePayments. You will receive a card in the mail with the first payment. You will need to activate the card over the phone. Each additional payment will be automatically added to your card.

You are responsible for paying state, federal, or other taxes for the payments you receive for being in this study. Taxes are not withheld from your payments.

What are my choices if I decide not to take part in this study?

Instead of participating in this study, you have some other choices.
You could:

- Not participate in this study or any other study
- Take part in another study

How will you keep my data safe and private?

We will keep information we collect about you confidential. We will share it with others if you agree to it or when we have to do it because U.S. or State law requires it. For example, we will tell somebody if you we learn that you are hurting a child or an older person.

We will put information from this study into your Electronic Medical Record (EMR). Your health care providers may be able to see that you participated in the study or had a procedure (e.g. skin biopsy) for the study. Additional results will not be visible. Other people or groups such as a health insurance company who have access to your EMR may see this information.

When your specimens and information are stored, we are careful to protect your identity from discovery by others. Strict security safeguards are in place to reduce the chance of misuse or unplanned release of information. Your information will be stored in a secured and password-protected database. Access to the database will be restricted to members of the research team. Any computers that store your electronic protected health information are encrypted, password-protected, and are on the secure Yale Network. Any printed health information is stored in locked file cabinets. Physical measures such as locks are also in place for desktop and laptop computers.

Whenever possible, the researchers will use your data without any pieces of information that can identify you (such as your name). Instead, they will assign a code to your clinical data record and specimens. Rarely, some studies may require that we use information that can identify you. If that happens, those studies must be first approved by the Yale Human Investigation Committee (HIC). The HIC is an ethics committee that reviews, approves and monitors research on human subjects.

When we publish the results of the research or talk about it in conferences, we will not use your name. If we want to use your name, we would ask you for your permission.

We will also share information about you with other researchers for future research but we will not use your name or other identifiers. We will not ask you for any additional permission. At the end of this study, if there are any samples remaining, we will make sure that all identifying information has been removed. After removal of identifiable information, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects. The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by NIH which is funding this project. You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

Genetic information will be shared using national databases that were designed so that researchers could store and use data and results from genetic studies that have investigated the interaction of genotype (a set of genes in your DNA which is responsible for a particular trait) and phenotype (the characteristics of that trait) in humans. A gene is the code in each cell in your body that controls the behavior of that cell. Parents pass the genes down to their children. Genes are responsible for many things about you such as eye color, hair color, blood type and hundreds of other traits. Future research may find out the details of how your DNA is put together. We may use your specimen for whole exome, genome sequencing, or genome wide association studies. That means we will look at all genes, not just those related to a specific disease. The cells may be injected into animals in some of the research. In some cases, this could mean that your cells and DNA could be preserved and used indefinitely for research purposes even if your original sample is no longer useful.

Your biospecimens (even if identifiers are removed) may be used for commercial profit and you will not share in this commercial profit.

What Information Will You Collect About Me in this Study?

The information we are asking to use and share is called “Protected Health Information.” It is protected by a federal law called the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA). In general, we cannot use or share your health information for research without your permission. If you want, we can give you more information about the Privacy Rule. Also, if you have any questions about the Privacy Rule and your rights, you can speak to Yale Privacy Officer at 203-432-5919.

The specific information about you and your health that we will collect, use, and share includes:

- The entire research record and any medical records held by Yale
- Records about phone calls made as part of this research
- Records about your study visits
- Information obtained during this research regarding
    - Physical exams
    - Laboratory and other test results

How will you use and share my information?

We will use your information to conduct the study described in this consent form.

We may share your information with:

- The study team. This includes the principal investigator, co-investigators, study coordinators and other members of the research team.
- Other researchers. These researchers may work for:
    - Yale
    - Universities, medical schools, or other research facilities
    - Government agencies, like the National Institute of Health
    - Public agencies, foundations or other groups that sponsor research
    - Companies that do research, like drug companies or biotechnology companies
- Representatives from Yale University and the Human Investigation Committee (the committee that reviews, approves and monitors research on human subjects), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- The U.S. Department of Health and Human Services (DHHS) agencies
- Healthcare providers who provide services to you in connection with the study
- Laboratories and other individuals and organizations that analyze your health information in connection with this study
- The U.S. Food and Drug Administration (FDA). This is done so that the FDA can review information about epinephrine and Lidocaine involved in this research. The information may also be used to meet the reporting requirements of drug regulatory agencies.

We will do our best to make sure your information stays private. But, if we share information with people who do not have to follow the Privacy Rule, your information will no longer be protected by the Privacy Rule. Let us know if you have questions about this. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

Why must I sign this document?

By signing this form, you will allow researchers to use and disclose your information described above for this research study. This is to ensure that the information related to this research is available to all parties who may need it for research purposes. You always have the right to review and copy your health information in your medical record.

What if I change my mind?

The authorization to use and disclose your health information collected during your participation in this study will never expire. However, you may withdraw or take away your permission at any time. You may withdraw your permission by telling the study staff or by writing to
Erin Longbrake, MD, PhD
PO Box 208018

New Haven, CT 06520.

If you withdraw your permission, you will not be able to stay in this study but the care you get from your doctor outside this study will not change. No new health information identifying you will be gathered after the date you withdraw. Information that has already been collected may still be used and given to others until the end of the research study to ensure the integrity of the study and/or study oversight.

Who will pay for treatment if I am injured or become ill due to participation in the study?

If you are injured while on study, seek treatment and contact the study doctor as soon as you are able.

Yale School of Medicine and Yale New Haven Hospital do not provide funds for the treatment of research-related injury. If you are injured as a result of your participation in this study, treatment will be provided. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available. You do not give up any of your legal rights by signing this form.

What if I want to refuse or end participation before the study is over?

Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits. Not participating or withdrawing later will not harm your relationship with your own doctors or with this institution.

To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part.

The researchers may withdraw you from participating in the research if necessary, for example, if you are unable to follow through with required study visits.

What will happen with my data if I stop participating?

Any information or samples previously collected about you as part of the research study will remain in the research record. No additional information about you will be collected after you stop participating.

Who should I contact if I have questions?

Please feel free to ask about anything you don't understand.

If you have questions later or if you have a research-related problem, you can call the Principal Investigator at 203-287-6100.

If you have questions about your rights as a research participant, or you have complaints about this research, you call the Yale Institutional Review Boards at (203) 785-4688 or email hrpp@yale.edu.

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.

Authorization and Permission

Your signature below indicates that you have read this consent document and that you agree to be in this study.

We will give you a copy of this form.

Optional Fee Waiver

I would like to waive my stipend for participating in this research study.

Initials: _____ Date: _____

Participant Printed Name	Participant Signature	Date
Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date