Permission to Take Part in a Human Research Study

Title of Research Study: *People with Multiple Sclerosis treated with Ocrelizumab and GLP-1 agonists*

Principal Investigator: Farrah Mateen, MD, PhD

Supported By: This research is supported by Genentech, Inc.

Financial Interest Disclosure: The following disclosure is made to give you an opportunity to decide if this relationship will affect your willingness to participate in this research study:

The study sponsor does not have any role in the conduct of the study or the decision to publish the results. The project was independently designed by the investigator.

If your doctor is also the person responsible for this research study, please note that your doctor is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether to participate in the research.

Key Information:
The first few pages of this document include a summary of this study to help you decide whether or not to participate. Detailed information is provided after the summary.

Why am I being asked to take part in this research study?

It is your decision whether or not to join this research study. We are asking you to be in this study because you are diagnosed with multiple sclerosis (MS), are currently being treated with Ocrelizumab, and either planning to start or already being treated with a glucagon-like peptide-1 (GLP-1) agonist.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

This research is being done to understand the effects of combining two types of treatment medications, Ocrelizumab and GLP-1 agonists, on people living with MS. Ocrelizumab is an FDA-approved disease modifying treatment that's increasingly the treatment of choice for individuals with MS in the USA and globally. GLP-1 medications, also approved by the FDA, are commonly used to treat for diabetes and support weight management. Some research also suggests GLP-1 agonists could have neuroprotective, cardiovascular and/or weight maintenance benefits.

Despite the growing use of both medications in clinical care, there is currently very limited information about how these medications interact when treated together for individuals with MS. The study is being conducted to evaluate the safety, potential benefits, and progression of disease activity through the use of Ocrelizumab and GLP-1 at the same time for people with MS. In addition, further information on co-treatment best practices could help patients and providers feel more confident in continuing MS treatment without interruption of discontinuations.

How long will the research last, and what will I need to do?

We expect that you will be in this research study an estimation of 2 years. Your participation will continue until the final follow up data collection and depending on what study group you are a part of, the timeline will differ as well.

You will be asked to participate in study calls and complete surveys to report medication dosing, adherence, tolerability, weight, height, and exercise activities. In addition, the surveys will include self reported measures of fatigue, disability, mood, and quality of life. You will be monitored through various clinical assessments, including blood tests to check your general health and biomarkers of disease, and how well you are tolerating treatment. The study calls will be held every 6 months to make sure the study is going smoothly and verify medication and disease progression history.

You can find more detailed information about the study procedures in the **What happens if I say, "Yes, I want to be in this research"?** section.

Is there any way being in this study could be bad for me?

You may experience medication side effects, including both the Ocrelizumab and GLP-1 medications. You may also experience injection-site reactions which could be bothersome. Additionally, you may experience emotional distress or be psychologically burdened by repeated testing and surveying throughout the study.

You may be subject to an unforeseen data breach during the conduct of the study through data hacking or other means due to human error or technological problems.

You can find more detailed information about the risks of this study in the **Is there any way being in this study could be bad for me? (Detailed Risks)** section.

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits for future individuals living with MS include establishing the safety of GLP-1 agonists in Ocrelizumab-treated patients and evaluating progression independent of relapse activity. More data from patients taking both medications can help patients and providers make better, more informed decisions about treatment plans.

What happens if I do not want to be in this research?

Participation in research is completely voluntary. You decide whether or not to participate. If you choose not to participate, there will be no penalty to you or loss of benefit to which you are entitled.

Your alternative to participating in this research study is not to participate.

Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

Whom can I talk to?
If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team. Ask questions as often as you want. Farrah Mateen, MD, PhD is the person in charge of this research study. You can call her at 410-935-5181 (available M-F 9 am to 5 pm) or email her at farrah.mateen@northwestern.edu with questions about this research study. This research has been reviewed and approved by an Institutional Review Board (IRB). You may talk to them at (312) 503-1376 or irbcompliance@northwestern.edu if:

- The research team is not answering your questions, concerns, or complaints.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

How many people will be studied?
We expect about 100 people here will be in this research study.

What happens if I say, "Yes, I want to be in this research"?
If you choose to take part in this research study, you will be asked to sign and date this consent form before any study-related activites described below are performed. You will have the opportunity to ask the research team any questions if you need clarification.

Depending on your current ongoing medication treatments, you will be placed into one of two groups. One of the groups will allow you to be fully remote for your participation and you will not need to visit the study site in person or be independently mobile to participate. However, you must be continuously available during the study timeframe remotely for study related calls such as surveys. There will be blood draws in the second group's trial while group 1 has an optional blood draw component. Group 2 will be required to come in 5 separate, scheduled times for various clinical assessments and questionnaires. Each visit will approximately take 2-3 hours. For the blood test, there will be one required draw and the amount of blood drawn will range from 1 to 4 tablespoons (tbsp). You may be asked to return for an unscheduled visit (for example, if you experience a relapse or if you leave the study early). A blood sample may be required during these visits if necessary.

Once enrolled into the study, both groups will be asked to fill out various questionnaires. These questionnaires will happen on a monthly or quarterly basis and will include reports on medication dosing, adherence to medicine, tolerability, weight, height, and exercise activities. In addition, you will also be asked to self assess yourself on various scales that measure disability, fatigue, mood, and quality of life.

You will be contacted and interviewed via Zoom every 6 months to do ensure study procedures are going as planned, verify data reported on medication and MS disease history, and ensure

study procedures are operating smoothly. Participants who do not complete the surveys within 7 days of the scheduled timing will be contacted by a study coordinator by phone up to 3 times.

Schedule of Assessments of MS Participants: Frequency and Scale

	Screening	Baseline	Week 24	Week 48	Week 72 & 96	Unscheduled Visit (e.g. Relapse, Early Withdrawal)
Clinical & MS Relapse History	X	X	X	X	X	X
Medication Review	X	X	X	X		X
Physical Examination	X		X	X		X
Neurological Examination	X	X	X	X		X
EDSS[3] & Ambulation Score (clinician-rated disability)		X	X	X		X
Vital Signs (ht, wt, BMI, blood pressure, heart rate, respiratory rate)	X	X	X	X		X
PDDS (patient-reported disability/ambulation)		X	X	X	X	X
QOL54-MS (MS-specific quality of life)		X	X	X		X
25-foot timed walk test (walking speed/ambulation)		X	X	X		X
9-Hole Peg Test (manual dexterity)		X	X	X		X
SDMT (information processing speed)		X	X	X		X

NFL-2, plasma (for biomarkers of disease)		X	X	X	X	X
GFAP, blood (for biomarkers of disease)		X		X	X	
Urine pregnancy test	(X)	(X)	(X)	(X)		(X)
MRI Brain, 1.5T		X		X		X

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for:

- Completing surveys, participating in self-assessments, and providing various measures.
- If you are in Group 2, providing a blood sample once at the beginning of the study. If you are in Group 1, providing a blood sample is optional.
- Keeping in touch with the study team if there are any changes to your medication treatment regimen.

What happens if I say "Yes" but I change my mind later?

You can leave the research at any time; it will not be held against you.

If you decide to leave the research, contact the investigator so that the investigator can take the appropriate steps.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. Specifically, your choice not to be in this study will not negatively affect your right to any present or future medical treatment.If you withdraw from the study, any data collected until the time of your withdrawal will be retained for study related purposes. However, no additional data will be collected after this moment. You may request someone from the study team to remove your data.

Detailed Risks: Is there any way being in this study could be bad for me?

You may experience medication side effects, including both the Ocrelizumab and GLP-1 medications. Although these medications will be given in the context of clinical care for FDA approved indications, in particular, the GLP-1 class of medications is known to cause gastrointestinal symptoms. These symptoms can include nausea, vomiting, early satiety, and abdominal discomfort and they are considered reversible, common (approximately 1/3 of all people treated with a GLP-1 medicaiton), and expected. These risks are often mild to moderate and in some if the medications are poorly tolerated, it may lead to early discontinuation. You may also experience injection-site reactions which could be bothersome.

In addition, you may experience emotional distress or be psychologically burdened by repeated testing and surveying throughout the study.

You may be subject to an unforeseen data breach during the conduct of the study through data hacking or other means due to human error or technological problems. This may lead to inadvertent disclosure of the MS diagnosis to others. All available measures will be taken to avoid such incidents and warn participants of these risks during the consent process. This study involves the use of your identifiable, personal information, and there is a chance that a loss of confidentiality could occur. The researchers have procedures in place to lessen the possibility of this happening. See the section below titled: **"What happens to the information collected for the research?"**

We will do our best to protect your data and samples during storage and when they are shared. However, there remains a possibility that someone could identify you. There is also the possibility that people who are not supposed to might access your data and samples. In either case, we cannot reduce the risk to zero.

Will it cost me anything to participate in this research study?

Taking part in this research study will not lead to any costs to you.

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, the information gathered from the study can have possible benefits for future individuals living with MS. As well, the safety of GLP-1 agonists in Ocrelizumab-treated patients will be established through patient reported assessments, clinical data, and biomarker data. If GLP-1 agonists help protect against progression independent of relapse activity in individuals of the study, it could potentially lead to the development of a new treatment option for people living with MS. Lastly, more data from patients taking both medications can help patients and providers make better, more informed decisions about treatment plans.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study data and medical records, to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this institution.

We will not ask you about child [or elder] abuse, but if you tell us about child [or elder] abuse or neglect, we may be required or permitted by law or policy to report it to authorities.

The study may keep your biological samples for future research. Any remaining blood from the blood draw will be stored for future tests related to MS and metabolism that are not a part of the study's main goals. You will be asked if you agree to have your blood stroed at Northwestern University for future testing.

If identifiers are removed from your identifiable private information or identifiable samples that are collected during this research, that information or those samples could be used for future research studies or distributed to another investigator for future research studies without your additional informed consent. See the information found under **"Will my data or samples be used for future research?"**

The sponsor, monitors, auditors, the IRB, the Northwestern University Office for Research Integrity, the U.S. Office of Research Integrity (ORI), the U.S. Office for Human Research Protections (OHRP), and the U.S. Food and Drug Administration (FDA) may be granted direct

access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

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.

Will my data or samples be used for future research?

This study is collecting data and samples from you. We would like to make your data and samples available for other research studies that may be done in the future. The research may be about similar diseases or conditions to this study. However, research could also be about unrelated diseases, conditions, or other types of research. These studies may be done by researchers at this institution or other institutions, including commercial entities. Your data and samples may be shared with researchers around the world. Our goal is to make more research possible. We plan to keep your data and samples for 5 years after study completion. To get your data or samples, future researchers must seek approval from this institution, and review by an IRB may be required.

Your name and identifying information will be removed from any data and samples you provide before they are shared with other researchers. Researchers cannot easily link your identifying information to the data and samples.

What else do I need to know?

If you become ill or are injured as a result of this study (medications, devices, or procedures), you should seek medical treatment through your doctor or treatment center of choice. You should promptly tell the study doctor about any illness or injury.
The hospital [university, researchers] will not pay for medical care required because of a bad outcome resulting from your participation in this research study. This does not keep you from seeking to be paid back for care required because of a bad outcome.

If you agree to take part in this research study, for group 1 we will pay you 75 USD every 3 months for a total of up to 600 USD for your time and effort. For group 2, you will receive 150 USD in the first visit and 100 USD every subsequent visit occasions and then 150 USD at the final study visit with a total of up to 500 USD.

You will have the option to receive cash or a gift card.
The Accounting Services at Northwestern University will be given your name, address, and Social Security Number in order to issue a check for your study participation. Study payments are considered taxable income and reportable to the IRS. A Form 1099 will be sent to you if your total payments are $600 or more in a calendar year.

You will have access tol study results at the end of the study after the data are locked and the data are presented, including your clinical scores and bloodwork. Future test results, if additional tests are performed on stored blood samples, will be reported back to you only if the test results provide a possibility of clinical relevance to the participant.

HIPAA Authorization

We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Your health information we may collect and use for this research includes:

- Results of physical examinations
- Medical history
- Lab tests, or certain health information indicating or relating to a particular condition as well diaries and questionnaires
- Records about study medication or drugs
- Billing information

During this study, you may be coming to a Northwestern Memorial HealthCare/Northwestern Medicine entity for research appointments or to get clinical services, such as lab tests, needed for the study. When that happens, you will be scheduled for these services through the NMHC computer system. When a clinical exam or lab is done by NMHC or one of its employees for the purpose of this research study, that information will be kept in both NMHC's clinical records and in the study records.

The following clinical providers may give the researchers information about you: all current and previous health care providers, including but not limited to the Shirley Ryan AbilityLab (SRALAB) and Northwestern Memorial HealthCare/Northwestern Medicine entities and its current and future affiliates.

Once we have the health information listed above, we may share some of this information with the following offices or entities outside of Northwestern University and its clinical partners (or affiliates): the Northwestern University Institutional Review Board Office and Office for Research Integrity; the US Office of Research Integrity; the US Office for Human Research Protections; the US Food and Drug Administration.

Any research information shared with outside entities will not contain your name, address, telephone or social security number or any other personal identifier unless disclosure of the identifier is necessary for review by such parties or is required by law or University policy [except that such information may be viewed by the Study sponsor and its partners or contractors at the Principal Investigator's office].

The following entities may receive your health information:

- Authorized members of the Northwestern University workforce, who may need to see your information, such as administrative staff members from the Office for Research, Office for Research Integrity and members of the Institutional Review Board.
- Clinical affiliates, including but not limited to the Shirley Ryan AbilityLab (SRALAB), Northwestern Memorial HealthCare, and the Ann & Robert H. Lurie Children's Hospital of Chicago (Lurie Children's). Your participation in this clinical trial may be tracked in an electronic database and may be seen by investigators running other trials that you are enrolled in and by your healthcare providers.
- Clinical affiliates, including but not limited to Northwestern Memorial HealthCare, for purposes including, but not limited to, the affiliate's provision of care to you and/or the affiliate's scheduling of appointments and/or billing activities.

- Other University research centers and University contractors who are also working on the study,
- Study monitors and auditors who make sure that the study is being done properly,
- Genentech, who is sponsoring the study, and that company's contractors and partners.
- Government agencies and public health authorities, such as the Food and Drug Administration (FDA) and the Department of Health and Human Services (DHHS).

Those persons who get your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it. Some of those persons may be able to share your information with others without your separate permission.

Unless you revoke your consent, it will not expire.

Although you may revoke consent to participation in this research at any time and in any format, you must revoke authorization for use or disclosure of your health information in writing.

To revoke your authorization, write to:
PI's Name: Farrah Mateen, MD, PhD
Institution: Northwestern Medicine
Department: Neurology
Address: Morton Building 7-643
310 E. Superior St.
Chicago, IL 60611

You do not have to authorize the use or disclosure of your health information; however, you will not be allowed to take part in this research study. If you do not authorize the use or disclosure of your health information, it will not affect your treatment by health care providers, or the payment or enrollment in any health plans, or affect your eligibility for benefits.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

A copy of this signed consent document, information about this study, and the results of any test or procedure done may be included in your medical records and may be seen by your insurance company.

Optional Elements:

The following research activities are optional, meaning that you do not have to agree to them in order to participate in the research study. Please indicate your willingness to participate in these optional activities by placing your initials next to each activity.

Do you agree to the collection of your blood if assigned to be in group 1 of the research study? This will be a one time draw at the beginning of the study and the amount of blood drawn will range from 1 to 4 tablespoons (tbsp). You must visit the study site to have the blood collected.

Permission to Take Part in a Human Research Study

I agree	I disagree	
_____	_____	The researcher may ask if you are willing to get your blood drawn if you are placed in group 1 of the research study.

Signature Block for Adults Capable of Providing Consent:

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

_____ _____
Signature of Participant Date

_____
Printed Name of Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent