The UNIVERSITY OF CHICAGO
The Division of the Biological Sciences • The University of Chicago Medical Center

CONSENT/AUTHORIZATION BY SUBJECT FOR PARTICIPATION IN A RESEARCH PROTOCOL

Protocol Number: IRB16-1390
_____
_____

Name of Subject: _____
Medical History Number: _____

STUDY TITLE: **Effects of ACTHAR on advanced MRI surrogate markers of disease activity and on comprehensive immune signature during MS relapses**

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You are being asked to participate in a research study. A member of the research team will explain what is involved in this study and how it will affect you. This consent form describes the study procedures, the risks and benefits of participation, as well as how your confidentiality will be maintained. Please take your time to ask questions and feel comfortable making a decision whether to participate or not. This process is called informed consent. If you decide to participate in this study, you will be asked to sign this form.

WHY IS THIS STUDY BEING DONE?

You have been asked to participate in this research study because you have been diagnosed with MS and are undergoing an exacerbation of your symptoms. The cause of MS is unknown. New lesions are seen in the brain or spine in patients having an MS exacerbation. How these lesions repair after therapy over time is largely unknown. Also, it is not entirely clear how the immune system changes for the better after treatment of MS exacerbations. We hope to examine MRI and blood markers of damage and inflammation in patients undergoing MS exacerbations.

For the MS exacerbation, you will be given ACTHAR , which is an FDA approved drug for the treatment of MS exacerbations/relapses. ACTHAR has been shown to provide the same benefit in curtailing the symptoms of MS exacerbations, as does intravenous methylprednisolone. Both ACTHAR and IV methylprednisolone are routinely used in medical practice for the treatment of MS exacerbations/relapses.

We hope that the information we gather during this study will lead to better understanding of the disease process involved in MS, especially repair and lead to better treatments for MS exacerbations.

The study is being sponsored by Mallinckrodt and the data will be shared with them. Your name and any identifying information will be removed from these documents.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?
About 18 people will take part in this study at the University of Chicago.

WHAT IS INVOLVED IN THE STUDY?

Subjects will have a physical/neurological examination, blood pressure, height, weight, and temperature taken at the time of visits. Urine pregnancy test or urine analysis may be done if there is a clinical concern for pregnancy or urine infection. This will be based on the discretion of the investigators. Physical exams and EDSS will be performed at each study visit. EDSS is scoring of your neurological exam. ACTHAR will be given as daily subcutaneous injections over 10 days. You will be asked to allow a small amount of blood to be collected around the time of your study visit. Often during assessment of MS exacerbation, small amount of blood is drawn as a routine medical practice. You may be asked for a small amount of additional blood sample. The amount of blood taken is small, about 15-18 cc, which is approximately 2 tablespoons. Blood samples will be taken at the initial visit, last day of ACTHAR (day 10 of therapy), 1 month post 1st dose, and at months 3 and 6.

You will also be asked to undergo MRIs to thoroughly assess inflammatory activity in the brain and spine during an MS exacerbation. You will be asked to undergo additional MRI images that are more sensitive (yet experimental) than the MRI images for examining MS disease. The MRI has a routine clinical component and a research component. The routine clinical component will take about 20 minutes. The research component may take up to additional 45 minutes. Both scans are done on the same scanner and on the same day, right after one another. MRIs will be performed at the initial visit, 1 month after the 1st dose of ACTHAR, and at months 3, 6, and 12. During the MRI scan, you may receive an intravenous contrast agent that allows better visualization of pathological changes in the brain or spine. Your treating physician will discuss the risks of the contrast agent with you prior to the MRI session, and you may be asked to sign a separate hospital consent form for the MRI procedure. You will not receive any additional contrast agent for the purposes of this research.

If you do not have an adequate response to the ACTHAR administration after 14 days, you may either be given a choice of getting another round of ACTHAR for additional 10 days or switching to IV Methylprednisolone 1000 mg for 3 days.

During this study, your current MS medication will not change during the relapse. However, one month after the relapse (after the 1 month MRI time point and blood draw), the doctor and you will decide whether to continue your current MS medication over time or switch to a different MS medication. All medications will be recorded during the course of the study.

During this study, Dr. Adil Javed and his research team will collect information about you for the purposes of this research. Data will be collected from your medical records. The data includes the type and severity of your disease, lab tests, family history of related diseases, toxin exposures, your prior therapeutic drug use, your name, age, date of birth, sex, phone number, date of entry into the study, and medical record number in order to contact you with more questions or updates. Since the cause of the above listed medical conditions is unknown, all of these factors may be relevant in understanding the disease.

Study Schedule

	Screening -2 weeks	Baseline (day 1)	Day 10	Month 1	Month 3	Month 6	Month 12
Discussion of study criteria	x						
Review and sign Informed Consent Form	x						
Review your medical history and demographics	x						
Review changes in your health and medications	x	X	x	x	x	x	x
Physical examination	x	X	x	x	x	x	x
Height and weight	x	X	x	x	x	x	x
Blood pressure, pulse rate, breathing rate, body temperature	x	X	x	x	x	x	x
Blood sample (approximately 1–3 tablespoons at each visit) [a]	x	X	x	x	x	x	
EDSS assessment	x	x	x	x	x	x	x
MRI scans of your brain		X		x	x	x	x
Urine pregnancy test (if clinically indicated)	x	X	x	x	x	x	x

HOW LONG WILL I BE IN THE STUDY?

You may be in this study for up to 12 months.

Dr. Javed or his research team may decide to take you off of the study without your consent if:

- You are unable to meet the requirements of the study;
- Your medical condition changes;
- New information becomes available that indicates that participation in this study is not in your best interest; or
- If the study is stopped.

WHAT ARE THE RISKS OF THE STUDY?

Blood Draw Risks

The potential risks of drawing blood include a bruise at the site of the puncture. This happens occasionally. Very rarely, inflammation of the vein and infection has been reported. Care will be taken to avoid these complications.

MRI Risks
The potential risks of MRI include claustrophobia and risks associated with contrast agents. You may be given a mild sedative before MRI.
The research-related MRI scans are not being done for diagnostic purposes. If any abnormalities are noted during the research scans, your treating physician will be informed, and you will be instructed to discuss these findings with your treating physician.

There are no reports of any harmful effects to humans of the research MRI sequences proposed in this study.

Contrast Agent Risks
The potential risks of contrast agent include allergic reactions, these subjects will be excluded from the study. Also, pre-contrast renal function will be assessed prior to the contrast MRI. Hydration will be recommended after the MRI.

Potential risks for ACTH:

Potential risks for ACTH are listed in the package insert. Subjects will receive advice on the side effects as it is done in clinical practice. The most common side effects are water gain, injection site reaction, mild insomnia and flushing. These will be managed as per standard care.

Any time you participate in a research study, there is the potential for loss of confidentiality, meaning that somebody outside of the research team could learn about your participation in the study. To protect your confidentiality, the data we collect about you for this study, including your name and medical record number, will be kept in a locked room on a password-protected computer and will not be listed in publications.

ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?
Knowledge about the advanced MRI and blood markers of disease activity and repair may provide us with information about MS and may lead to better treatment of MS relapses in the future.

If you agree to take part in this study, there may or may not be direct medical benefit to you.

WHAT OTHER OPTIONS ARE THERE?
Instead of being in this study, you may choose not to participate. Participation is strictly on a volunteer basis and you may refuse at any time.

The decision whether or not you wish to participate in this study will not affect your care at the University of Chicago Medical Center.

WHAT ARE THE COSTS?

Clinical services provided during a clinical trial are either research-related or related to usual medical care. Research-related services are done to complete the research and the costs are not the responsibility of you or your insurance.

The costs that are considered research-related for this study may include any additional laboratory tests to assess your immune function, physician visits, physical/neurological exam, and research related MRIs that are dictated by the research protocol and are only required because you are taking a part in this study. The study drug ACTHAR will be provided free to you as long as you are in this study.

Usual medical care costs include any and all services that are considered medically necessary for your disease and would be done even if you were not part of this research study. This may include laboratory tests, physician visits, standard/routine MRIs, procedures, and other clinical services that your physician orders for your standard medical care. The cost of this usual, ongoing medical care will be the responsibility of you or your insurance, and may include deductibles and co-payments. Similarly, this care will be subject to all the same requirements and restrictions of your insurance.

If you have questions about whether specific clinical services are research related or usual medical care, please speak to your physician or research contact person. If you suffer an unanticipated injury as a direct result of this research and require emergency medical treatment, the University of Chicago Medical Center will provide such treatment at the University of Chicago Medical Center at no cost to you. You must notify Dr. Javed as promptly as possible after your injury in order to receive this care. An injury is "unanticipated" if it is not one of the known effects of a study drug, medical device or procedure, and is not the result of your disease or condition. The costs of any non-emergency care for such an injury will be billed to you or your insurance in the ordinary manner. If you think that you have suffered a research related injury, you must let Dr. Javed know right away.

WILL I BE PAID FOR MY PARTICIPATION?
You will not be paid to participate in this study.

WHAT ABOUT CONFIDENTIALITY?
Study records that identify you will be kept confidential. Your name and medical record number will be kept in a locked room on a password-protected computer and will not be listed in publications. The data will be accessible by Dr. Javed, and people directly working with him. Your identity will not be known or available to anyone outside the research team. This information will not be part of your medical record.

The data collected in this study will be used for the purpose described in the form. By signing this form, you are allowing the research team access to your medical records, which include Protected Health Information. Protected Health Information (PHI) consists of any health information that is collected about you, which could include your medical history and new information collected as a result of this study. The research team includes the individuals listed on this consent form and other personnel involved in this study at the University of Chicago.

As part of the study, Dr. Javed and his research team may report the results of your study-related procedures and tests to Mallinckrodt outside of the University of Chicago. This information would include data from your blood and spinal fluid tests and MRI along with relevant factors related to your history such as age, gender, and type of disease. Please note that your information will be assigned a code before being sent to any of the collaborators. Only the research team at the University of Chicago will be able to link the code to your name.

Your records may be reviewed by federal agencies whose responsibility is to protect human subjects in research including the Food and Drug Administration (FDA) and Office of Human Research Protections (OHRP). In addition, representatives of the University of Chicago, including the Institutional Review Board, a committee that oversees the research at the University of Chicago, may also view the records of

the research. If your research record is reviewed by any of these groups, they may also need to review your entire medical record.

The results from experimental tests and/or MRI procedures performed as part of this study will not be part of your medical record. Only the standard clinical blood work and standard clinical MRI results will be shared with you. However, if the experimental immune tests and non-standard MRIs show clinically significant abnormalities, Dr. Javed or his research team will contact you and discuss any necessary evaluation.

During your participation in this study, you will have access to your medical record. Dr. Javed is not required to release to you research information that is not part of your medical record.

Data from this study may be used in medical publications or presentations. Your name and other identifying information will be removed before this data is used. If we wish to use identifying information in publications, we will ask for your approval at that time.

This consent form will be kept by the research team for at least six years. The study results will be kept in your research record and be used by the research team indefinitely. At the time of study completion, either the research information not already in your medical record will be destroyed or information identifying you will be removed from study results.

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 any time.

WHAT ARE MY RIGHTS AS A PARTICIPANT?
Taking part in this study is voluntary. If you choose not to participate in this study, your care at the University of Chicago/University of Chicago Medical Center will not be affected.

You may choose not to participate at any time during the study. Leaving the study will not affect your care at the University of Chicago/University of Chicago Medical Center.

If you choose to no longer be in the study and you do not want any of your future health information to be used, you must inform Dr. Javed in writing at the address on the first page. Dr. Javed may still use your information that was collected prior to your written notice.

We will tell you about significant new information that may affect your willingness to stay in this study.

You will be given a signed copy of this document. This consent form document does not have an expiration date.

WHO DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?
You have talked to your doctors about this study and you had the opportunity to ask questions concerning any and all aspects of the research. If you have further questions about the study, you may call Dr. Javed at 773-834-0558.

If you have any questions concerning your rights in this research study you may contact the Institutional Review Board, which is concerned with the protection of subjects in research projects. You may reach the Committee office between 8:30 am and 5:00 pm, Monday through Friday, by calling (773) 702-6505 or by writing: The University of Chicago, Institutional Review Board, 5841 S. Maryland Ave., MC-7132, I-625, Chicago, Illinois 60637.

CONSENT

SUBJECT:
The research project and the procedures associated with it have been explained to me. The experimental procedures have been identified and no guarantee has been given about the possible results. I will receive a signed copy of this consent form for my records.

I agree to participate in this study. I am aware that my participation is voluntary and that I do not have to sign this form if I do not want to be part of this research study.

Signature of Subject: _____
Date: _____ Time: _____ AM/PM (Circle)

PERSON OBTAINING CONSENT
I have explained to _____ the nature and purpose of the study and the risks involved. I have answered and will answer all questions to the best of my ability. I will give a signed copy of the consent form to the subject.

Signature of Person Obtaining Consent: _____
Date: _____ Time: _____ AM/PM (Circle)

INVESTIGATOR/PHYSICIAN:

Signature of Investigator/Physician _____
Date: _____ Time: _____ AM/PM (Circle)

10/23/2019