Informed Consent Form

Memantine for the Treatment of Cognitive Impairment in Systemic Lupus Erythematosus (ClearMEMory)

NCT03527472

Dated 12/8/2021

Vanderbilt University Institutional Review Board
Informed Consent Document for Research

Principal Investigator: Leslie Crofford, M.D. **Revision Date: 12/23/18**
Study Title: A randomized, double-blind, placebo-controlled phase 2 clinical trial of memantine for the treatment of cognitive impairment in systemic lupus erythematosus
Institution/Hospital: Vanderbilt University Medical Center

This informed consent applies to adults with Systemic Lupus Erythematosus.

Name of participant: _____ Age: _____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. Your medical record will contain a note saying you are in a research study. Anyone you authorize to receive your medical record will also get this note.

1. What is the purpose of this study?

You are being asked to take part in this research study because you have systemic lupus erythematosus (SLE or lupus) and have problems related to thinking, memory, attention, mood or other indicators of neuropsychiatric SLE (NPSLE). The purpose of this study is to evaluate the safety and effectiveness of the drug memantine in treating the symptoms of NPSLE over the course of three months. Memantine is approved by the US Food & Drug Administration (FDA) for the treatment of moderate to severe dementia in people with Alzheimer's disease, but memantine is considered investigational for the purposes of this study. We are seeking to understand whether memantine, which stops a protein in the body shown to be involved in NPSLE, will improve your symptoms. In addition, we will see if some people with NPSLE have a higher level of certain antibodies (NMDA receptor antibodies) that may cause problems with thinking, and if these antibodies make a difference in who will respond to treatment with memantine. After you finish the study, we will look at your medical records, review the results of our testing, and conduct additional laboratory studies on your blood samples to determine if there are similarities among the patients who improved with memantine treatment. This information will help to better identify patients who may benefit from memantine treatment. Approximately 144 people with NPSLE will be evaluated at Vanderbilt University Medical Center to determine if they are eligible to take part in this study. We expect that approximately ½ of the people we screen will be eligible to enter the treatment study.

2. What will happen and how long will you be in the study?

If you agree to be in this study, we will ask you to come to the Vanderbilt Clinical Research Center (CRC) for an initial screening visit and three study visits over three months. Total expected duration of your participation is 14 weeks. At the screening visit, we will ask you about your medical history to be sure you are eligible to be in the study. We will draw some blood tests to be sure it will be safe for you to take memantine. You will also undergo testing to be sure that you have measurable problems with your thinking. If we cannot measure the problems you are having we will not be able to enroll you in the study. At each of the three study visits, blood samples will be taken to measure laboratory values that are important for monitoring your safety. Urine samples will be taken at two of the three study visits as an additional measure of safety. We will also ask you a series of questions about your SLE symptoms and you will complete questionnaires and tests to help us measure things like anxiety and depression. If you are a woman who could become pregnant, we will ask you for a urine sample to test for pregnancy.

Over the course of the study, you will take pills by mouth twice a day each day. You will receive a medication diary and instructions how to document each time you take the pills. This is a randomized, double-blind, placebo-controlled study

which means that you will either receive pills containing the drug memantine or pills that do not contain the drug (placebo). You will not know which type of pills you receive and no one on the study team will know which pills you are being given. No one is able to choose who receives which type of pill, and so it is entirely due to random chance which type of pill you will receive. You will increase the dose of memantine or placebo every week for the first 4 weeks as tolerated. If you begin having side effects that you cannot tolerate we will reduce your dose or take you out of the study.

If you have 1) recently changed medications that may affect thinking or mood, 2) regularly use certain medications including drugs of abuse, 3) are pregnant, 4) have any severe psychiatric diseases including schizophrenia, psychosis, or suicidal depression, 5) have a history of certain types of brain injury, or 6) have severe liver or kidney disease, you will not be allowed to be in this study. You will also not be allowed to be in this study if you are taking certain medicines including amantadine, carbonic anhydrase inhibitors (e.g., acetazolamide), dextromethorphan, ketamine, or sodium bicarbonate because they may increase the risk of memantine's side effects. If you are a woman who could become pregnant, we will ask you for a urine sample to test for pregnancy. We will ask you about your medical history to be sure you are eligible to be in the study.

We will also collect and store blood specimens to be used for research. These samples will be stored by a unique number, not by your name.

Your samples may be made available to others to use for research. To protect your privacy, we will not release your name or any other information that might identify you. You will not receive any benefit as a result of the tests done on your samples. These tests may help us learn more about the causes, risks, or prevention of thinking problems or other manifestations of lupus.

Your samples may be used to make new treatments or tests. These may have value and may be developed and owned by the study staff, Vanderbilt University Medical Center, and/or others. If this happens, there are no plans to provide money to you.

Please check Yes or No to the questions below:

My blood may be used for research.

☐ Yes ☐ No

My blood may be stored/shared for future research in lupus or other autoimmune diseases.

☐ Yes ☐ No

My blood may be stored/shared for future research for other health problems (such as cancer, heart disease, etc.).

☐ Yes ☐ No

You may contact me for future studies of lupus or other autoimmune diseases.

☐ Yes ☐ No

In the future, your samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples in other studies.

Screening Visit

This visit will take approximately 3 hours. You will come into the CRC where we will ask you some questions about your medical history, conduct a physical exam, take your blood pressure and weigh you. We will collect urine and blood samples and you will complete some tests that measure your thinking, memory, attention and mood. The blood and urine taken during this visit will be used to perform laboratory tests to help determine if you qualify to move on to the drug study. We will also collect blood for research that will also be used to determine if you have NMDA receptor antibodies and for other lupus research. We will approximately take 3 tablespoons (up to 45 ml) of blood from your arm.

Patients that meet final eligibility criteria for this study will move forward to the drug treatment study. If you are eligible for the study, a study coordinator will call you to schedule the first study visit, which will take place approximately two weeks after the screening visit.

Study Visits 1, 2, and 3

You will come to the CRC for each study visit. The morning of each visit, you will take your regular medications (if any).

At study visit 1 you will receive pills containing memantine or placebo, which you will begin taking every day for a total of 12 weeks. We will start with a low dose and increase the dose for the first 4 weeks of treatment. Study visit 2 will take place 6 weeks after study visit 1. Between study visits 1 and 2, a study coordinator will contact you weekly by phone, email or text according to your preference to ask you if you are taking the study drug as instructed and ask if you are experiencing any side effects from the study drug. These calls will allow us to determine if we can increase your dose of memantine or placebo. Study visit 3 will take place 6 weeks after study visit 2. Between study visits 2 and 3, a study coordinator will contact you every other week by phone, email or text to ask if you are experiencing side effects from the study drug.

At each of the three study visits you will undergo a medical history and physical exam and provide blood samples. You will provide urine samples at two of the three study visits. At the third study visit, you will undergo the same tests from the screening visit that measure thinking, memory, attention and mood. Study visits 1 and 2 will take approximately 2 hours, and study visit 3 will take approximately 3 hours. We will take approximately 1-2 tablespoons (up to 8.5 ml at visits 1 and 2, and 15.5 ml at visit 3) of blood from your arm at each of the three study visits.

You will be free to stop participating in the study at any time. Any information provided up until the time you withdraw may be used in the study.

3. Costs to you if you take part in this study:

There is no cost to you for taking part in this study.

4. Side effects and risks that you can expect if you take part in this study:

There are certain risks associated with taking the study drug, memantine. These risks include:

Common (≥5% and Higher Frequency than Placebo)

Confusion, constipation, dizziness, headache

Uncommon (At least 2% and Higher Frequency than Placebo)

Fatigue, pain, hypertension, vomiting, back pain, somnolence (sleepiness), hallucinations, coughing, dyspnea (shortness of breath),

Risks Identified After FDA Approval

Low blood counts, heart failure, pancreatitis (inflammation of the pancreas), hepatitis (inflammation of the liver), suicidal ideation, acute renal failure (kidney failure), allergic skin rash.

Pregnancy

Memantine is classified as an FDA pregnancy risk. There are no adequate and well-controlled studies in pregnant women. If you are a female who could get pregnant, we will do a urine pregnancy test to make sure you are not pregnant. If you are pregnant, you will not be able to be in the study.

Additional Risks

There are minor risks and discomforts associated with blood draws. We will insert a small needle into the vein to draw blood. This may cause a brief period of pain and possibly a small bruise at the site. Occasionally, a person feels faint when their blood is drawn. There is a small risk of bleeding after removal of the needle and possibly a bruise at the site, which can be prevented by tight compression on the site. Rarely, an infection develops which can be treated. We will use careful and sterile techniques to minimize these side effects.

You may experience stress and discomfort due to the effects of participating in cognitive and psychological screening tests. This discomfort is typically mild and transient, if it does occur.

There may be risks that we do not know about at this time. If we should find out any new information, we will notify the participants.

5. Payment in case you are injured because of this research study:

If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided **at Vanderbilt** to treat the injury.

There are no plans for Vanderbilt to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

6. Good effects that might result from this study:

a.) The benefits to science and humankind that might result from this study: We may learn about using memantine as a new treatment for certain symptoms of NPSLE. However, there is no guarantee that you will benefit from being in this research. Additionally, if you are randomized to be in the group of participants taking the placebo pills then it is unlikely you will experience any benefits from taking those pills.

b.) The benefits you might get from being in this study: You may experience an improvement in certain symptoms of your NPSLE. You may also not benefit from participating in this study.

7. Other treatments you could get if you decide not to be in this study:

You can choose not to be in this study, and nothing about your health care will change.

8. Payments for your time spent taking part in this study or expenses:

You will be paid for your time for being in this research study ($50 for the screening visit and visits 2-3, $100 for visit 4). You will be paid for each visit you complete including the screening visit even if you do not qualify for the treatment study. You will need to provide your social security number (SSN) in order for us to pay you. You may choose to participate without being paid if you do not wish to provide your SSN for this purpose. You will also need to provide your address so that a check can be mailed to you. Your SSN is obtained for payment purposes only and it will not be retained for research purposes. It may take up to 4-6 weeks to receive your check following completion or withdrawal from the study.

If you live outside Davidson County, travel to the study center may be reimbursed. Mileage expenses will be reimbursed at the current standard federal mileage rate of 54.5 cents per mile per occurrence.

9. Reasons why the study doctor may take you out of this study:

You will be withdrawn from the study if the study doctors decide it is best for you. If the study doctors withdraw you from the study, you will be told the reason.

10. What will happen if you decide to stop being in this study?

If you decide to stop being part of the study, you should tell your study doctor. Deciding to not be part of the study will not change your regular medical care in any way.

11. Who to call for any questions or in case you are injured:

If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact Jonathan Williams, PhD (Study Coordinator) at 615-875-9200 or Leslie Crofford, MD (Principal Investigator) at 615-322-4746.

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the Vanderbilt University Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

12. Clinical Trials Registry:

A description of this clinical trial will be available on 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.

13. Confidentiality:

All efforts, within reason, will be made to keep your personal information in your research record confidential but total confidentiality cannot be guaranteed. The study results will be kept in your research record for at least six years after the study is over for as long as we need the information for the study. All the information on paper will be kept locked in a

secure location. Any information kept in a computer will be through REDCap or the Vanderbilt CRC data system, which has many safeguards. Only members of Dr. Crofford's research team will be able to see any of the information that would identify you. Any research data entered into your medical record will be kept as long as it is needed.

Vanderbilt may share your information, without identifiers, to others or use it for other research projects not listed in this form. Vanderbilt, Dr. Crofford and her staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

This study may have some support from the National Institutes of Health (NIH). If so, your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

14. Authorization to Use/Disclose Protected Health Information

All efforts, within reason, will be made to keep your protected health information (PHI) private. PHI is your health information that is, or has been, gathered or kept by Vanderbilt as a result of your healthcare. This includes data gathered for research studies that can be traced back to you. Using or sharing ("disclosure") such data must follow federal privacy rules. By signing the consent for this study, you are agreeing ("authorization") to the uses and likely sharing of your PHI. If you decide to be in this research study, you are also agreeing to let the study team use and share your PHI as described below.

As part of the study, Vanderbilt University Medical Center may share the results of your study and/or non-study linked test results from your medical record, as well as other parts of your medical record, to the groups named below. These groups may include people from the Federal Government Office for Human Research Protections, the VUMC Institutional Review Board, and Vanderbilt University. Federal privacy rules may not apply to these groups; they have their own rules and codes to assure that all efforts, within reason, will be made to keep your PHI private.

The study results will be kept in your research record for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will be kept for an unknown length of time.

Unless told otherwise, your consent to use or share your PHI does not expire. If you change your mind, we ask that you contact Dr. Jonathan Williams, in writing and let him know that you withdraw your consent. His mailing address is:

Jonathan Williams, PhD
[redacted]

Principal Investigator: Leslie Crofford, M.D. **Revision Date: 12/23/18**
Study Title: A randomized, double-blind, placebo-controlled phase 2 clinical trial of memantine for the treatment of cognitive impairment in systemic lupus erythematosus
Institution/Hospital: Vanderbilt University Medical Center

At that time, we will stop getting any more data about you and discard any remaining blood samples. But, the health data we stored before you withdrew your consent may still be used for reporting and research quality.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

Date _____ Signature of Patient/Volunteer _____

Consent obtained by:

Date _____ Signature _____

Printed Name and Title _____ Time _____

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