Rivastigmine for Antimuscarinic Delirium: a Randomized, Placebo-controlled Trial

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Washington University in St. Louis

INFORMED CONSENT DOCUMENT

Project Title: Rivastigmine for antimuscarinic delirium (RIVA-AM): a randomized, placebo-controlled trial

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Research Team Contact: Emergency Care Research Core
(314) 305-1054

If you are the parent/guardian providing parental permission the word "you" refers to your child.

If you are the legally authorized representative providing consent the word "you" in this document refers to the person you represent.

This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights and responsibilities as a research participant.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We invite you to participate in this research study because you have been diagnosed with antimuscarinic delirium (AMD), a kind of confusion caused by certain overdoses and poisonings.

The purpose of this research study is to determine whether a medication called rivastigmine can help you recover from this condition faster than usual care. In order to determine this, we are comparing rivastigmine to a placebo in this study. You may receive rivastigmine or a placebo as part of your participation in this study. A placebo is a substance that looks like the study drug but contains no active medication (like a sugar pill). You have a 50/50 chance of being assigned to either rivastigmine or placebo.

Rivastigmine is being investigated as a treatment for AMD because it has a chemical action similar to that of physostigmine, a drug that has been used for many years for the treatment of AMD but that now is in short supply.

Rivastigmine is approved by the U.S. Food and Drug Administration (FDA) to treat dementia due to Alzheimer's disease and Parkinson's disease. Rivastigmine is not approved by the FDA for treatment of antimuscarinic delirium or for use in children. The use of rivastigmine is considered investigational in this study.

WHAT WILL HAPPEN DURING THIS STUDY?

A research coordinator will come to your bedside and evaluate your level of wakefulness or sedation by speaking to you, observing your behavior, and attempting to wake you up if you are sleeping or not responding to questions. The research coordinator will also ask you a couple of questions to determine if you are confused. Based on this assessment, we will decide if you are eligible to continue to participate in the study.

If you are eligible to participate, you will be randomly assigned (like the flip of a coin) by computer to be treated with rivastigmine or a placebo. You will be given the medication to which you are assigned. Your doctors and nurses will not know which medication you are given but can find out if needed for safety reasons.

If you are still confused or agitated after the first dose of medication, your doctor can decide to give you another dose. You may receive up to three doses of medication after the first one for a total of 4 doses.

You will be admitted to the hospital for ongoing care as part of your general medical care (that is, care that is not part of the research study). While you are admitted to the hospital, a research team member will come to your room and re-evaluate you every 2 hours. On each re-evaluation, the research team member will evaluate your level of wakefulness or sedation by speaking to you, observing your behavior, and attempting to wake you up if you are sleeping or not responding to questions. The research team member will also ask you a couple of questions to determine if you are confused. If you are able to talk to the team member, they will ask you some questions about how you are feeling. They will also talk to your nurse about how you have been doing since the last time you were assessed.

The research team will stop re-evaluating you after you have been recovered from your condition with no signs of agitation or confusion for 8 hours, or when you are discharged from the hospital, whichever comes first. If you remain in the hospital after recovering, we will re-evaluate you daily to check on how you are doing.

Afterwards, we will review your medical record chart in the computer and look at some information about your diagnosis and treatment. This information will include your age, sex, race and ethnicity, diagnosis, vital signs, weight and height, and urine drug screen results (if applicable). We will also look at the medications you were given in the hospital, the symptoms you experienced in the hospital, the location(s) where you received your care, and amount of time you spent in the hospital.

We will not add any information to your medical record. No information from the study will be placed in your medical chart.

Will you save my research information to use in future research studies?

The data we are obtaining in this study may be made available for studies going on right now as well as studies that are conducted in the future. These studies may be done by researchers at Washington University, other research centers and institutions, or private companies involved in research.

We may also share your research data with large data repositories (a repository is a database of

information) for use by others, such as the research community, institutions, private companies and other researchers. If your individual research data is placed in one of these repositories, your name and other identifying information will be removed. All reasonable precautions will be taken to protect your privacy and confidentiality. Necessary approvals will be obtained to use the data. Certain summary information may be available to the general public.

These future studies may provide additional information that will be helpful in understanding antimuscarinic delirium or other diseases or conditions, including research to develop investigational tests, treatments, drugs or devices that are not yet approved by the U.S. Food and Drug Administration. Should this occur, there are no plans to provide financial compensation to you. There are no plans to provide financial compensation to you should use of your data occur. It is unlikely that what we learn from these studies will have a direct benefit to you. By allowing us to use your data you give up any property rights you may have in the data**.** We will protect the confidentiality of your information to the extent possible.

Your data will be stored without your name or any other kind of link that would enable us to identify which sample(s) or data are yours. Therefore, it will be available indefinitely for use in future research studies without your additional consent and cannot be removed.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 42 people will take part in this study conducted by investigators at Washington University.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for the duration of your admission to the hospital for this condition. You will be actively monitored by our research staff as described above until you have been consistently recovered for a total of 8 hours. Further monitoring of your health data by review of the medical record will continue until you are discharged from the hospital. After you are discharged from the hospital, the study will be over and there will be no further contact, monitoring, or research activities.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Some risks described in this consent document, if severe, may cause death.

If you are randomized to receive a placebo, you will not receive treatment with rivastigmine. If you do not participate in the trial, it is possible, although not certain, that your doctors may choose to treat you with rivastigmine. Agreeing to participate in the study means that there is a risk that you might not receive rivastigmine.

Risks of rivastigmine:

Less Likely / Less Common

Serious

- Low heart rate

Mild

- Stomach pain, nausea, vomiting, or diarrhea

Rare

Serious

- Seizure
- Very low heart rate
- Low heart rate with low blood pressure

Women Capable of Becoming Pregnant

If you are a woman capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. Because this study will take place only in the hospital, we do not anticipate that you will become pregnant during the study. If you are pregnant when you enroll in the study, there may be unknown risks to your unborn child, or risks to your unborn child that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to an unborn child. If you believe you are pregnant while participating in this research study, please contact the research team member identified at the top of this document as soon as possible.

Breach of Confidentiality

One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure. Please see the section in this consent form titled *"How will you keep my information confidential?"* for more information.

WHAT ARE THE BENEFITS OF THIS STUDY?

You may or may not benefit from being in this study.

However, we hope that, in the future, other people might benefit from this study because it will allow us to determine if rivastigmine is effective in treating antimuscarinic delirium, which will allow us to provide higher-quality evidence-based treatment to future patients with this condition.

WHAT OTHER TREATMENT OPTIONS ARE THERE?

Before you decide whether or not to be in this study, your doctor will discuss the other options that are

available to you. Instead of being in this study, you could opt to be treated according to our usual local practice of care. The local practice of care may or may not involve administration of rivastigmine, which is sometimes given to patients with antimuscarinic delirium at this hospital. The local practice of care may also involve other sedative medications to help calm you down or medical observation alone.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any additional costs for being in this research study.

You and/or your medical/hospital insurance provider will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?

You will not be paid for being in this research study.

WHO IS FUNDING THIS STUDY?

The American Academy of Clinical Toxicology (AACT) is funding this research study. This means that Washington University is receiving payments from the American Academy of Clinical Toxicology to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from the American Academy of Clinical Toxicology for conducting this study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

Washington University investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator at (314) 273-1109 and/or the Human Research Protection Office at 1-(800)-438-0445.

Decisions about whether payment for medical treatment for injuries relating to your participation in research will be made by Washington University. If you need to seek medical care for a research-related injury, please notify the investigator as soon as possible.

HOW WILL YOU KEEP MY INFORMATION CONFIDENTIAL?

Other people such as those listed below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you. We will keep your participation in this research study confidential to the extent permitted by law.

- Government representatives (including the Office for Human Research Protections) to complete federal or state responsibilities
- The U.S. Food and Drug Administration
- The American Academy of Clinical Toxicology
- Hospital or University representatives to complete Hospital or University responsibilities

- Information about your participation in this study may be documented in your health care records and will be available to anyone with access to your health care record, including your health insurance company. This information may also be released as part of a release of information request.
- The last four digits of your social security number may be used in hospital or University systems to track billing information for research procedures.
- Washington University's Institutional Review Board (a committee that oversees the conduct of research involving human participants) and the Human Research Protection Office. The Institutional Review Board has reviewed and approved this study.

Any report or article that we write will not include information that can directly identify you. The journals that publish these reports or articles require that we share your information that was collected for this study with others to make sure the results of this study are correct and help develop new ideas for research. Your information will be shared in a way that cannot directly identify you.

To help protect your confidentiality, we will link your information to a unique study identifier number and use that number to identify you on most research materials instead of your name, date of birth, or other identifying information. Your number will be linked to your name and identifying information on an encrypted spreadsheet stored on a secure electronic system, with access limited to people working on the study. All research materials with any information about you will be stored on a secure electronic system with access limited to people working on the study. This link will be destroyed once the study has ended and your information will become anonymized.

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.

Are there additional protections for my health information?

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form. The research team will follow state and federal laws and may share your health information with the agencies and people listed under the previous section titled, "How will you keep my information confidential?".

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form or as permitted or required by law. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University's Privacy Officer at 866-747-4975.

Although you will not be allowed to see the study information, you may be given access to your health care records by contacting your health care provider.

If you decide not to sign this form, it will not affect

- your treatment or the care given by your health provider.
- your insurance payment or enrollment in any health plans.
- any benefits to which you are entitled.

However, it will not be possible for you to take part in the study.

If you sign this form:

- You authorize the use of your PHI for this research
- This authorization does not expire.
- You may later change your mind and not let the research team use or share your information (you may revoke your authorization).
  - To revoke your authorization, complete the withdrawal letter found in the Participant section of the Human Research Protection Office website at hrpo.wustl.edu.
    - **If you revoke your authorization:**
      - The research team may only use and share information already collected for the study.
      - Your information may still be used and shared as necessary to maintain the integrity of the research, for example, to account for a participant's withdrawal from the research study or for safety reasons.
      - You will not be allowed to continue to participate in the study.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed.

If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I decide to withdraw from the study?

You may withdraw by telling the study team you are no longer interested in participating in the study or you may send in a withdrawal letter. A sample withdrawal letter can be found in the Participant section of the Human Research Protection Office website at hrpo.wustl.edu.

If you decide to leave the study early, we will ask you to tell research staff or your bedside nurse right away. They will contact the research team and ensure that you are withdrawn from the study. If you withdraw from the study, you will not receive any more study drug (rivastigmine or placebo) and you will not undergo any more bedside re-evaluations. Your care will otherwise continue as usual, as directed by your treating physicians.

If you withdraw from the study we will ask your permission to continue to collect information from your health care records.

Will I receive new information about the study while participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can someone else end my participation in this study?

Under certain circumstances, the investigator might decide to end your participation in this research study earlier than planned. This might happen for no reason or because in our judgement it might no longer be safe for you to continue in the study.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Emergency Care Research Core, (314) 305-1054. If you experience a research-related injury, please contact: Kevin Baumgartner, (314) 273-1109. If you need to contact someone urgently, you can call the research coordinator on call at (314) 305-1054 and tell them you are participant in the RIVA-AM study.

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office at 1-(800)-438-0445, or email hrpo@wustl.edu. General information about being a research participant can be found on the Human Research Protection Office web site, hrpo.wustl.edu. To offer input about your experiences as a research participant or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study. As a participant you have rights and responsibilities as described in this document and including:

- To be given enough time before signing below to weigh the risks and potential benefits and decide if you want to participate without any pressure from the research team or others.
- To understand all of the information included in the document, have your questions answered, and receive an explanation of anything you do not understand.
- To follow the procedures described in this document and the instructions of the research team to the best of your ability unless you choose to stop your participation in the research study.
- To give the research team accurate and complete information.
- To tell the research team promptly about any problems you have related to your participation, or if you are unable to continue and wish to stop participating in the research study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

Do not sign this form if today's date is after EXPIRATION DATE: 04/08/25.

_____ _____
(Signature of Participant) (Date)

_____
(Participant's name – printed)

Parent/Guardian Name and Relationship to Participant:

Do not sign this form if today's date is after EXPIRATION DATE: 04/08/25.

_____
(Child's name – printed)

_____ _____
(Signature of Parent/Guardian) (Date)

_____ _____
(Name of Parent/Guardian- printed) (Relationship to participant – printed)

Legally Authorized Representative's Name and Relationship to Participant:

Do not sign this form if today's date is after EXPIRATION DATE: 04/08/25.

_____
(Participant's name – printed)

_____ _____
(Signature of Legally Authorized Representative) (Date)

_____ _____
(Name of Legally Authorized Representative - printed) (Relationship to Participant – printed)

Who should sign as the Legally Authorized Representative (LAR)?
If the participant has a legal guardian or attorney-in-fact this individual must sign as the LAR.

If there is no legal guardian or attorney-in-fact the individuals listed below may sign in order of priority.

(1) Spouse unless the participant has no spouse, or is separated, or the spouse is physically or mentally incapable of giving consent, or the spouse's whereabouts is unknown or the spouse is overseas;
(2) Adult child;
(3) Parent;
(4) Brother or sister;
(5) Relative by blood or marriage.

Statement of Person Who Obtained Consent

The information in this document has been discussed with the participant or, where appropriate, with the participant's legally authorized representative. The participant has indicated that they understand the risks, benefits, and procedures involved with participation in this research study.

_____ _____
(Signature of Person who Obtained Consent) (Date)

_____
(Name of Person who Obtained Consent - printed)