Maximizing trEatment of Neurological Dysfunction using INtravenous Guanfacine (MENDING) study

NCT 04742673

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VUMC Institutional Review Board
Informed Consent Document for Research

Study Title:	Maximizing trEatment of Neurological Dysfunction using INtravenous Guanfacine (MENDING) study
Version Date:	12/5/2022
PI:	Christopher G. Hughes, MD, MS

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.

Key Information:
The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Key information about this study:
We are asking you to take part in this study that looks at whether guanfacine administered into your IV (small tube in your vein) can treat confusion in patients in the ICU, called ICU delirium. If you agree to participate, and begin to become confused while in the ICU, we will give you guanfacine or placebo (fluid without any active medication). We will also collect data while you are in the hospital. Some of this data will come from you or your surrogate. We will also contact you with questions three different times after you leave the hospital. These visits will happen approximately 1, 3, and 6 months after you leave the hospital. We will also draw small amounts of blood twice while you are in the hospital. We will try to draw blood from tubes already in your vein or artery to minimize discomfort. There is no cost to you to take part in the study. The risks of guanfacine include sleepiness, tiredness, nausea, dry mouth, low blood pressure, and stomachache. One other risk is loss of privacy. We have strong measures in place to protect participant privacy like storing data on secure servers and in locked rooms. You may benefit directly if guanfacine helps reduce your delirium or confusion but this is not guaranteed.

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

You are being asked to take part in this research study because you are critically ill in the intensive care unit (ICU) at high-risk for having delirium, a type of confusion that happens a lot with ICU patients.

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This confusion (delirium) is common, and we don't know how best to prevent or treat it. Delirium can lead to longer hospital stay, a higher chance of death, and an increased risk of long-term thinking problems. There is no medicine proven or approved to treat delirium, yet many different drugs are used. The purpose of this study is to learn if a drug called guanfacine works to treat this delirium. In this study, you will be randomly assigned, like the flip of a coin, to 1 of 2 groups. One group will receive guanfacine in an intravenous (IV) catheter which is a small tube in your vein used to administer medicines and fluids. One group will receive placebo (a clear liquid with no drug) in an IV catheter. The Food and Drug Administration (FDA) has given permission to the investigators to give the study drug through your IV instead of in your mouth or through a tube in your nose or mouth. The study will monitor how this drug affects confusion (delirium) and thinking. Guanfacine is approved by the FDA to treat other medical conditions and is used by many doctors to treat delirium. But, it is not yet known whether guanfacine is effective for confusion (delirium) in the ICU, and it is not approved by the FDA to treat this confusion, making its use investigational in this study. Some patients have thinking and memory problems after they leave the ICU. We also want to learn if guanfacine can lessen memory and thinking problems for patients who go home from the hospital. About 100 patients will take part in this study at Vanderbilt. You will be followed for the duration of your hospital stay and for approximately 6 months after you start receiving study drug (phone only after you leave the hospital).

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 and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

Side effects and risks that you can expect if you take part in 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.

<u>Guanfacine</u>
Common side effects (Affects between 1 in 100 and 1 in 10 people): drowsiness, tiredness, nausea, dry mouth, low blood pressure, stomachache.
Uncommon or rare side effects (affects between 1 in 10,000 and 1 in 100 people): confusion, slow heart rate, headache, constipation, vomiting, weakness, allergic reaction.

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Most of these side effects are reported to occur less often and are of less severity than other agents commonly used to treat patients for agitation and confusion in the ICU. The study drug will only be administered while you are in the ICU, have confusion, do not have too low of blood pressure or heart rate, and are on close monitoring for your current illness. Thus, while receiving study drug, you will be closely monitored for these side effects. The ICU clinical team will be immediately available to manage any side effects if seen, and the study team will decrease the dose of study drug and/or stop study drug if these side effects are seen.

Drawing Blood

There are no major risks associated with drawing blood. You may experience minor discomfort, bruising or soreness from the needle. Sampling from a needle very rarely causes infection. Blood draws will be done by a trained professional. We will usually take blood from tubes that are already in your vein or artery. If you do not have a tube in a vein or artery, then we will get the blood with a needle. Pain, redness, soreness, bruising, or infection may occur at the needle stick site. Rarely some people faint. The study doctor may put some cream (called EMLA) on your skin to numb the area so you will not feel the needle stick as much. The numbing cream may make your skin or the area have a change in skin color, but this is rare.

Follow-up Phone-call Assessments

Assessments of your thinking, quality of life, and physical function may be tiring for some individuals. To minimize this possible discomfort, breaks are encouraged and scheduled within the session. In the event that you appear to be under too much strain, sessions will be discontinued. The small possibility exists that you may experience a degree of emotional discomfort related to learning about the existence or severity of thinking problems.

Loss of Privacy

Participation in any research study, including this one, may involve a loss of privacy, and absolute confidentiality cannot be guaranteed. To minimize this risk, all information collected on paper will be kept in locked file cabinets. Information collected on computer will be password protected and stored on a secure network. All data keys will be stored separately and securely. Only study personnel will have access to the study data.

Risks that are not known:

Because this treatment is investigational, meaning non-FDA approved, there may be risks that we do not know about at this time.

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Good effects that might result from this study:
The benefits to science and humankind that might result from this study: We hope this helps us find ways to treat delirium in ICU patients.

The benefits you might get from being in this study: You may or may not directly benefit (i.e., less confusion or thinking problems) if you receive guanfacine in this study.

Procedures to be followed:

When you are in the ICU, this will happen:

- We will collect information about your age, sex, race, and your past and present medical history. We will ask your family questions about your previous activities of daily living and ability to think clearly.
- You will be assessed twice a day for confusion.
- Your sedation and pain management will be handled just as it is normally by your doctors.
- You will receive other interventions and monitoring to prevent and manage delirium, which include stimulation of thinking, use of hearing aids/glasses, pain level monitoring, sleep hygiene, and muscle exercises.
- Female patients of childbearing potential will receive a pregnancy test for research only, if you have not already had one completed for routine care. If the pregnancy test is positive, you will be excluded from the study.

If you become confused and develop delirium, this will happen:

- You will be randomly assigned to one of the 2 study groups. You have an equal chance of getting assigned to either of the groups. You, your family, the clinical teams, and the study staff will not know to which drug you have been assigned. Only the pharmacy will know whether you have been assigned to receive guanfacine or placebo.
- For research only, while you are in the ICU and confused, you will receive study drug through your IV for up to 14 days, or until you leave the ICU (whichever happens first).
- You will be monitored closely for any side effects from the medications (slow heart rate, low blood pressure, decrease wakefulness, etc.). You will also be monitored for other things that influence confusion: labs, vital signs, other medications, physical activity, and sleep problems.
- The first 2 days you are confused, we will draw some blood for research only (using already existing lines in your vein when possible, to avoid extra blood sticks) to evaluate changes in your blood. The amount of blood collected will be less than 1½ tablespoons each time, for a

total of 3 tablespoons. For all other laboratory values, we will use whatever your doctor has ordered.

When you get out of the ICU, this will happen:

- We will collect information about your hospital course.
- You will be assessed once a day for confusion.
- Before hospital discharge you will be asked some questions about your ability to think clearly and your experiences in the ICU.
- You will be followed by phone for approximately 6 months after you start to receive study drug. We will call you at 1 month, 3 months, and 6 months to ask about your ability to think clearly, your quality of life, and your mobility and function. This should take about 1 hour.

Importantly, a small percentage of patients enrolled in the study will never become confused, so they will never receive study drug or follow up phone calls.

If you agree to participate in this study, we will save your contact information and contact you about future studies.

Overview table of study activities

Activity	Enrollment	In the hospital	After hospital discharge
Collect baseline health and activity information	X		
Collect information about your current illness and hospital course		X	
Assess for confusion	X	Daily	
Guanfacine or placebo administration (if you have confusion)		Daily up to 14 days	
Blood draws		Days 1 and 2	
Safety assessments		Daily	
Telephone questions about thinking, quality of life, physical function			1, 3, and 6 months

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Payments for your time spent taking part in this study or expenses:
If you are enrolled and randomized to receive study drug, you will be paid for participation in this study. After you return home from the hospital, you will receive $25 for completing the follow-up phone call assessment at 1 month, $25 for completing the follow-up phone call assessment at 3 months, and $25 for completing the follow-up phone call assessment at 6 months. The total compensation you may receive is up to $75.

Costs to you if you take part in this study:
If you agree to take part in this research study, you and/or your insurance will not have to pay for the tests and treatments that are being done only for research. However, you are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

You have the right to ask what it may cost you to take part in this study. If you would like assistance, financial counseling is available through the Vanderbilt Financial Assistance Program. The study staff can help you contact this program. You have the right to contact your insurance company to discuss the costs of your routine care (non-research) further before choosing to be in the study. You may choose not to be in this study if your insurance does not pay for your routine care (non-research) costs and your doctor will discuss other treatment plans with you.

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.

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 Dr. Christopher Hughes at (615) 936-6268. 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 VUMC Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

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Reasons why the study doctor may take you out of this study:
The study doctor may take you out of this study if his/her judgment suggests that is better for you. This decision may be based on new information about your condition or the study risks and benefits. If you are taken out of the study, you will be told the reason.

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. If you decide to stop being part of the study, we may continue to access your medical record to complete study follow-up. If you choose to withdraw your consent for us to access your medical record, we ask that you contact Dr. Christopher Hughes in writing to let him know. His mailing address is 1211 21st Avenue South, 422 MAB, Nashville, TN 37212.

Clinical Trials Registry:
A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time.

Confidentiality:
The information collected about you during the research study will be securely stored in the Critical Illness, Brain Dysfunction, and Survivorship (CIBS) Center at Vanderbilt University Medical Center. Your personal information will not be shared. You will be assigned a study ID number upon enrollment in the study. All data will be entered into a secured password protected database. Only study staff will be able to access study records. The research samples of blood will be stored in a secured location at Vanderbilt University Medical Center by Dr. Hughes and his research staff indefinitely. Blood samples will be coded so that identifiable information cannot be linked back to the samples without access to the code key. This code will be securely stored in CIBS Center and accessible only to study staff.

This study has support from the National Institutes of Health (NIH), and 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.

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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.

Privacy:
Any 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. These tests may help us or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems. Your samples may be used to make new products or tests. These may have value and may be developed and owned by the study staff, Vanderbilt University, Vanderbilt University Medical Center, and/or others. If this happens, there are no plans to provide money to you.

Study Results:
There are no plans to share study results with participants.

Authorization to Use/Disclose Protected Health Information
What information is being collected, used, or shared?
To do this research, we will need to collect, use, and share your private health information. All efforts, within reason, will be made to keep your information private. By signing this document, you agree that your health care providers (including both Vanderbilt University Medical Center and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use or share the information?
The people who may request, receive or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Vanderbilt, for example if needed for your clinical care or study oversight. By signing this form, you give permission to the research team to share your information with others outside of Vanderbilt University Medical Center. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If

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your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Do you have to sign this Authorization?
You do not have to sign this Authorization, but if you do not, you may not join the study.

How long will your information be used or shared?
Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

What if you change your mind?
You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator, Dr. Christopher Hughes, in writing to let them know by using the contact information provided in this consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

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.

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STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

Patient/Volunteer INITIAL Self Consent:

☐ **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.**

Patient/Volunteer RE-CONSENT after prior surrogate consent:

☐ **My legal representative gave his/her consent for me to be in this research study. This is because I was not able to make decisions on my own due to my illness. My condition has now improved. I am now being asked to decide whether to continue to be in this study. My decision is voluntary. This means the decision is up to me. I have read this consent form and the research study has been explained to me verbally. All my questions have been answered. My decision to continue is checked below:**

☐ **I agree to continue in the study.**
☐ **I do not agree to continue in the study.**

Signatures:

Patient/Volunteer	Date (mm/dd/yy)	
Witness (only needed if Patient/Volunteer is physically unable to sign for self)	Print name and title	Date (mm/dd/yy)
Person Obtaining Consent	Print name and title	Date (mm/dd/yy)

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Health Care Decision-Maker/Surrogate Consent

I, _____ [name of decision-maker/surrogate],

am the _____ [state relationship to participant]

of _____ [state participant's name].

I have read the informed consent document or it has been explained to me. I have had the opportunity to ask any questions and all of my questions have been answered. I have been informed that an investigational treatment may be administered to _____ [participant's name]. I believe receiving such treatment would be in the interests of _____ _____ [participant's name] and is consistent with what he/she would have decided had he/she been able to do so.

Your decision to allow your family member/friend to participate in this research study is voluntary. You may choose not to allow his/her participation and he/she will receive alternative treatments without affecting his/her healthcare/services or other rights. You are also free to withdraw him/her from this study at any time. In the event new information becomes available that may affect the risks or benefits associated with this research study or your willingness to allow continued participation in this research study, you will be notified so that you can make an informed decision whether or not to continue your family member/friend's participation in this study.

Your family member/friend will periodically be re-evaluated for the capacity to give consent. If he/she is found to be capable, continued participation in this study would only occur with his/her consent.

Signatures:

_____	_____
Health Care Decision-Maker/Surrogate	Date (mm/dd/yy)

_____	_____	_____
Person Obtaining Consent	Print name and title	Date (mm/dd/yy)