VANDERBILT UNIVERSITY
MEDICAL CENTER

November 20, 2023

ClinicalTrials.gov PRS – Protocol Registration and Results System

Re: NCT03865940 – Unique Protocol ID: TN – Efficacy of Guanfacine and Lidocaine Combination in Trigeminal Nerve Block for Pain Management in Trigeminal Neuropathy

IRB-approved Informed Consent Document

Study Title: **A Randomized, Double-Blind, 2-Way Crossover Trial to Assess the Efficacy of Guanfacine and Lidocaine Combination versus Lidocaine Alone in Trigeminal Nerve Block for Pain Management in Painful Trigeminal Neuropathy Patients**

Version Date: 06/22/2022

PI: **David Edwards, M.D. Ph.D.**

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.

What is the purpose of this study?

You are being asked to take part in this research study because you have painful trigeminal neuropathy. The purpose of this study is to compare the safety and effectiveness of the drug guanfacine in combination with the drug lidocaine to the safety and effectiveness of lidocaine alone in treating the symptoms of painful trigeminal neuropathy. Guanfacine is approved by the US Food & Drug Administration (FDA) for the treatment of hypertension or attention deficit hyperactivity disorder (ADHD), but guanfacine is considered investigational for the purposes of this study. We are seeking to understand whether guanfacine will improve your symptoms when given together with lidocaine therapy. After you finish the study, we will look at your medical records to determine if there are similarities among the patients who improved with guanfacine treatment. This information will help to better identify patients who may benefit from guanfacine treatment. Approximately 80 people with painful trigeminal neuropathy will be evaluated at Vanderbilt University Medical Center to determine if they are eligible to take part in this study. We expect to enroll 80 subjects with about 34 completing the full study.

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:

There are certain risks associated with taking the study drug guanfacine. Based on the known side effects of the study drug, the following risk associated with participation in the study are perceived as low:

- Bradycardia (slow heart rate)
- Hypotension (low blood pressure)
- Dry Mouth
- Sedation

Study Title: **A Randomized, Double-Blind, 2-Way Crossover Trial to Assess the Efficacy of Guanfacine and Lidocaine Combination versus Lidocaine Alone in Trigeminal Nerve Block for Pain Management in Painful Trigeminal Neuropathy Patients**

Version Date: 06/22/2022

PI: **David Edwards, M.D. Ph.D.**

- Dizziness
- Headache
- Bruising, redness, itching, or swelling at the site of injection
- Intravenous injection resulting in seizure or stroke
- Bleeding
- Increased pain

Pregnancy

Guanfacine is classified as FDA pregnancy category B. This means that animal studies have failed to demonstrate a risk to the fetus and 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.

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. There is no human or animal data regarding the safety of guanfacine for nerve block injection in combination with lidocaine.

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 guanfacine as a new adjunct treatment for painful trigeminal neuropathy.

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

Procedures to be followed:

If you agree to be in this study, we will ask you to come to the Vanderbilt Pain Clinic for an initial screening visit and two procedure visits. Total expected duration of your participation is 5-8 weeks. At the screening visit, we will ask you about your medical history to be sure you are eligible to be in the study. You will report your pain intensity and quality of life on standardized surveys. If your pain intensity does not score at or above a pre-determined threshold, we cannot enroll you in the study.

Following the screening visit, there will be two procedure visits during the study. During the first procedural visit you will receive with an injection of lidocaine alone or an injection of lidocaine plus the investigational drug guanfacine. You will not know which injection you receive, and no one on the study

team will know which injection you receive. You will be randomized 1:1 like the flip of a coin. After the injection procedure, you will report the intensity of your pain on a scale of 1-10 every 30 minutes for 8 hours and then daily for 14 days. You will have the option to record pain scores in a paper diary or using an easy text messaging system. If your pain is rated at a pre-determined threshold at the end of those 14 days, you will attend study visit 3 to receive your second injection. This injection will be the opposite treatment from what you received at study visit 2. Following the second injection you will again rate your pain intensity every 30 minutes for 8 hours and then daily for 14 days.

If your pain is below the pre-determined threshold at the end of the first 14 day period following study visit 2, study staff will periodically reach out to you to evaluate if your pain exceeds the pre-determined threshold. If your pain exceeds the pre-determined threshold, you may then be scheduled for study visit 3 and the study will proceed as described above. However, you will be discontinued from the study and will not attend study visit 3 and receive the second injection if your pain does not meet the predetermined threshold.

Your reports of how your pain changes in response to the investigational drug will be used to develop knowledge that may improve the treatments for painful trigeminal neuropathy. To protect your privacy, we will not release your name or any other information that might identify you.

Screening Visit

This visit will take approximately 1 hour. You will come into the Pain Clinic where we will ask you some questions about your medical history, conduct a physical exam, take your blood pressure, weigh you, and get an initial pain intensity rating. If you are a woman who could become pregnant, we will ask you if you believe you could be pregnant. If it is possible that you are pregnant, you will be ineligible for this study. We will ask women who could become pregnant to commit to using 2 forms of birth control throughout the duration of the study. We will review recent MRI or CT imaging to ensure safety of the nerve block injection. If no recent imaging exists, this will be ordered as part of standard care prior to nerve block.

Patients that meet final eligibility criteria for this study will move forward to the procedural visits. If you are eligible for the study, a study coordinator will work with you during your visit to schedule procedure visit 1, which will take place approximately one week after the screening visit.

Procedure Visits 1 and 2

At procedure visit 1, you will be asked to report your pain intensity and you will receive a nerve block injection of either the investigational drug (guanfacine + lidocaine) or the active control (lidocaine only).

Study Title: **A Randomized, Double-Blind, 2-Way Crossover Trial to Assess the Efficacy of Guanfacine and Lidocaine Combination versus Lidocaine Alone in Trigeminal Nerve Block for Pain Management in Painful Trigeminal Neuropathy Patients**

Version Date: 06/22/2022

PI: **David Edwards, M.D. Ph.D.**

At procedure visit 2, you will report your pain intensity and receive the opposite injection that you received at study visit 1. If you are a woman who could become pregnant, you will undergo a urine pregnancy test before each injection. 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. You will be monitored for pain intensity at 30-minute time intervals for the first 8 hours after block and then monitored once daily at the same timepoint for 14 days using a text message generated using REDCap (or if needed a paper diary).

2-3 weeks after your first procedure visit you will return to the clinic to receive the other treatment injection at your second procedure visit. Once again, you will be monitored for pain intensity at 30-minute time intervals for the first 8 hours after block and then monitored once daily at the same timepoint for 14 days.

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 per procedure visit). 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 gift card will 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 gift card following completion or withdrawal from the study.

Costs to you if you take part in this study:
There is no extra cost to you for taking part in this study.

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.

Study Title: **A Randomized, Double-Blind, 2-Way Crossover Trial to Assess the Efficacy of Guanfacine and Lidocaine Combination versus Lidocaine Alone in Trigeminal Nerve Block for Pain Management in Painful Trigeminal Neuropathy Patients**

Version Date: 06/22/2022

PI: **David Edwards, M.D. Ph.D.**

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 Patty Hendricks, RN (Study Coordinator) at 615-936-2831 or David Edwards, MD/PhD (Principal Investigator) at 615-343-9419.

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.

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.

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.

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 website at any time.

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 Pain Clinic, which has many safeguards. Only members of Dr. Edward'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. Edwards and his 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.

Study Title: **A Randomized, Double-Blind, 2-Way Crossover Trial to Assess the Efficacy of Guanfacine and Lidocaine Combination versus Lidocaine Alone in Trigeminal Nerve Block for Pain Management in Painful Trigeminal Neuropathy Patients**

Version Date: 06/22/2022

PI: **David Edwards, M.D. Ph.D.**

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.

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.

Study Results:

Study results will be published in medical journals and submitted to www.clinicaltrials.gov as described above. Published study results will not include information that can identify you; at most, publications will include a summary of the results.

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. 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).

Study Title: **A Randomized, Double-Blind, 2-Way Crossover Trial to Assess the Efficacy of Guanfacine and Lidocaine Combination versus Lidocaine Alone in Trigeminal Nerve Block for Pain Management in Painful Trigeminal Neuropathy Patients**

Version Date: 06/22/2022

PI: **David Edwards, M.D. Ph.D.**

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 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 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.

Study Title: **A Randomized, Double-Blind, 2-Way Crossover Trial to Assess the Efficacy of Guanfacine and Lidocaine Combination versus Lidocaine Alone in Trigeminal Nerve Block for Pain Management in Painful Trigeminal Neuropathy Patients**

Version Date: 06/22/2022

PI: **David Edwards, M.D. Ph.D.**

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: _____