Protocol Title: Diltiazem in Jervell and Lange-Nielsen Syndrome
Date: 5/17/2024
NCT06534671

Study Title: Diltiazem in Jervell and Lange-Nielsen Syndrome
Version Date: 5/17/2024
PI: Prince J. Kannankeril, MD,MSCI

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:
This study will test the effect of diltiazem, a calcium channel blocking drug, on the QT interval in patients with Jervell and Lange-Nielsen syndrome. If you participate, you will come to the Clinical Research Center and have an IV placed. The medicine will be given over 2 minutes and we will watch the QT interval on multiple ECG's taken over 20 minutes. You will be monitored in the Clinical Research Center for 2 hours after the medication, then the study is over. You will not need to fast or stop any of your usual medications for this study. There are no study procedures after the single study visit. There may be no benefit to you for participating in the study.

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 have a rare condition called Jervell and Lange-Nielsen (JLN) syndrome. This results in a very long QT interval and risk for arrhythmias. New experimental evidence suggests that diltiazem may shorten the QT interval in JLN syndrome. Diltiazem is FDA-approved for atrial arrhythmias, high blood pressure and chest pain, but it's use in JLN syndrome has not been described.

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

Study Title: Diltiazem in Jervell and Lange-Nielsen Syndrome
Version Date: 5/17/2024
PI: Prince J. Kannankeril, MD,MSCI

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:

Possible risks of the IV (intravenous) catheter: Putting a needle or catheter (tube) into your vein may cause bleeding, bruising, or infection (uncommon). We will use careful and sterile technique to minimize these side effects.

Possible risks of the EKG (electrocardiogram): To measure your heart rate an electrocardiogram (ECG) will be done. This is a test that records the electrical activity of the heart. You will be asked to lie down and sticky patches will be fixed to your chest. You will be asked to lie still. The sticky pads used for th e ECG may cause skin irritation.

One possible side-effect of IV (intravenous) diltiazem is low blood pressure (hypotension). Hypotension was the most commonly reported adverse event in other clinical trials, with symptomatic hypotension occurring in 3.2% of patients. Your blood pressure will be closely monitored on the study day and diltiazem will not be given if your blood pressure is low.

Other events reported in a least 1% of diltiazem-treated patients were:

Injection site reactions (e.g., itching, burning) - 1.7%,
Arrhythmia (junctional rhythm or isorhythmic dissociation) - 1%.

In addition, the following events were reported infrequently (less than 1%):

Cardiovascular – Asystole (heart stops beating), atrial flutter, AV block first degree (heart rhythm changes), AV block second degree (hear rhythm changes), chest pain,
congestive heart failure, sinus pause (heart rhythm changes), sinus node dysfunction (heart rhythm changes), syncope (fainting), ventricular arrhythmia, ventricular fibrillation, ventricular tachycardia

Dermatologic – Pruritus (itching), sweating

Gastrointestinal - Constipation, elevated SGOT or alkaline phosphatase (elevated liver enzymes), nausea, vomiting

Nervous System – paresthesia (numbness and tingling)

Study Title: Diltiazem in Jervell and Lange-Nielsen Syndrome
Version Date: 5/17/2024
PI: Prince J. Kannankeril, MD,MSCI

Other – Amblyopia (eye crossing), asthenia (pain), dry mouth, dyspnea (shortness of breath).

Allergic reactions to diltiazem are rare, and you will not be enrolled if you have a known allergy to diltiazem.

Risks that are not known:
There may be risks with diltiazem in JLN syndrome that we do not know about at this time.

Good effects that might result from this study:
The benefits to science and humankind that might result from this study: We may learn that diltiazem is useful in treatment of JLN syndrome.

Procedures to be followed:
All study procedures will occur in a single outpatient visit to the Clinical Research Center (CRC). You will take your regular medications. The study will be explained to you by a member of the study team upon your arrival to the CRC, and if you agree to participate, an IV will be placed in order to deliver medication during the testing. Weight and blood pressure will be checked along with a urine pregnancy test for subjects who might be pregnant. If you have an ICD, it will be interrogated. Electrodes will be placed on your chest for an ECG.

Diltiazem (0.25 mg/kg) will be given IV over 2 minutes. A repeat ECG and BP will be checked at 2, 5, 7, 10, 15 and 20 minutes. If the QT interval shortens, as expected, that will end the test, and you will be monitored in the CRC for 2 hours before being discharged.

If at 10 minutes the QT interval has not shortened, and your blood pressure is stable (systolic BP within 20% of baseline BP and > 100 mm Hg), an ECG and BP will be checked at 14 minutes and a repeat dose of diltiazem (0.35 mg/kg IV) will be given at 15 minutes. A repeat ECG and BP will be checked at 17, 20, 22, 25, 30 and 35 minutes and the study will end. You will be monitored in the CRC for 2 hours before being discharged.

The total time commitment is approximately 3 consecutive hours.

Payments for your time spent taking part in this study or expenses:
You will not be paid for taking part in this study.

Costs to you if you take part in this study:

Study Title: Diltiazem in Jervell and Lange-Nielsen Syndrome
Version Date: 5/17/2024
PI: Prince J. Kannankeril, MD,MSCI

There is no 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.

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. Prince Kannankeril at [redacted]. If you cannot reach the research staff, please page the study doctor at [redacted].

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.

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:
All records are retained on password-protected computers accessible only to members of the study team. Computers containing these records are only connected to networks if they include appropriate firewalls and security measures. The identity of any individuals and their families are not to be revealed in any publication without their written informed consent.

Study Results:
Study results will be shared with you if you so choose.

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

Study Title: Diltiazem in Jervell and Lange-Nielsen Syndrome
Version Date: 5/17/2024
PI: Prince J. Kannankeril, MD,MSCI

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 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.

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.

Study Title: Diltiazem in Jervell and Lange-Nielsen Syndrome
Version Date: 5/17/2024
PI: Prince J. Kannankeril, MD,MSCI

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 _____