

Clinical Study number: TCH-006

Sponsor: Theranica Bio-Electronics, Ltd.

Lead Principal Investigator: Dr. TBD, MD

Study title: An open label, single arm, multicenter study assessing the efficacy and safety of Nerivio, a remote electrical neuromodulation device, for acute treatment of migraine in people with chronic migraine

RESEARCH PARTICIPANT INFORMATION AND CONSENT FORM

Site:

Address:

TITLE: An open label, single arm, multicenter study assessing the efficacy and safety of Nerivio, a remote electrical neuromodulation device, for acute treatment of migraine in people with chronic migraine

PROTOCOL NO.: TCH-006
NCT04194008

SPONSOR: Theranica Bio-Electronics, Ltd.

INVESTIGATOR: XXXXXXXXXXXXX

**STUDY-RELATED
PHONE NUMBER(S):**

What you should know about a research study:

- This consent form will explain the purpose, the procedures, the risks and possible benefits of taking part in this research study. Please review it carefully.
- The main goal of regular medical care is to help each patient. The main goal of a research study is to learn things to help future patients.
- We cannot promise that participation in this research study will help you.
- Your participation in this research study can result in side effects that are explained below.
- Someone from the research team will explain this study to you. Make sure all your questions are answered before you make a decision.
- Your participation in this study is voluntary. You may decide not to participate, or you may leave the study at any time.
- The quality of your medical care will be the same whether you join, decline, or decide to leave the study.

Why is this study being done and what is its purpose?

This research is being done in order to evaluate a new treatment for people with chronic migraines.

You are being asked to participate in this study because you are suffering from chronic migraines.

The purpose of this study is to assess the effects of a neurostimulator device called the Nerivio device. The Nerivio device has been approved for treatment of acute migraine in non-chronic patients. This study intends to investigate the ability of the device for acute treatment of migraine in chronic patients.

The Nervio device is a non-invasive neuromodulation device operated via a smartphone application. The device is worn on the upper arm, and the treatment is self-administered at the onset of a migraine attack. The device delivers non-painful electrical pulses to the skin that stimulate the body to initiate a pain inhibition mechanism in the brain. During the treatment, the users can adjust the intensity of the pulses according to how they tolerate it.

How many people will take part in this study?

About 120 participants will be in this research study in the USA and Israel, with up to 25 participants from this site.

How long will you be in the study?

We expect that you will be in this research study for about 16 weeks.

Who is doing the research study?

Dr. _____ is in charge of this research study at _____.

What can I expect if I take part in this research study?

You will receive the Nerivio device, and a smartphone application will be installed on your smartphone to control the device and record your feedback regarding its effect on your migraine. During the treatment, you will be able to adjust the intensity of pulses according to your tolerability to the electrical pulses.

If you agree to be in the study:

- You will have to answer questions regarding your migraine in order to determine whether you are eligible to participate in the study.
- You will need to answer questions regarding your general medical condition in order to determine whether you are eligible to participate in the study.
- You will need to fill out questionnaires regarding you migraine and quality of life
- If you are a female of childbearing potential, a urine sample for pregnancy test will be taken.

Study Chart and Timelines

If you agree to take part in this study, you will have up to 4 study visits.

Visit 1- you will start at enrollment. During the enrollment we will assess your eligibility to participate in the study and you will need to sign this Informed Consent Form. Following your consent to participate in this study, the study coordinator will collect your medical and migraine information and you will be asked to complete a baseline questionnaire. You will receive training on how to operate the application in order to report your migraine diary during the run-in stage.

The **Run-in stage** will last for 4 weeks. During this stage you will be requested to report the onset of all your migraines and headaches. The report should always be made within 60 minutes of pain start. Once a report is made, a baseline questionnaire will appear on the app, and you will be requested to record your pain intensity level, the presence/absence of aura and associated migraine symptoms (nausea, light sensitivity, sound sensitivity, and touch sensitivity) as well as your stress levels and your ability to perform usual activities. You will also be asked to answer these questions at 2 hours and 24 hours post initial report, with the addition of medication usage information.

At the end of this stage you will be requested to return to the clinic in order to move forward to the treatment stage.

Visit 2- You will receive training on how to operate the device using the application, and we will assist you to determine the level of intensity that is the best for you as a "well felt, but not painful" intensity. In addition, you will be trained how to complete the migraine diary during migraine attacks. At the end of this visit you will receive 2 devices to take home with you and to treat your chronic migraines.

The **Treatment stage** will last for 4 weeks. During this stage you will be requested to carry the Nerivio device and the smartphone with the application with you at all times, in order to be able to apply and operate the device immediately after your migraine symptoms or headache appears, and no later than 60 minutes from onset.

You will need to avoid any migraine rescue medication from the time of onset until 2 hours following the beginning of the treatment (the time of reporting the 2h migraine diary within the application). This is extremely important, because the purpose of the study is to measure the impact of the device. Any rescue medication consumed with the device sabotages the ability of the researchers to make any conclusions about the device

Please note:

- These requirements are crucial to the success of the study. If you feel that you will not be able to comply with these requirements (carry the device with you all the time, apply the device as soon as you feel your migraine symptoms and avoid migraine rescue medication for 2h after starting the treatment), please consider your participation in the study and inform us about your hesitations.
- During the study, you may receive text messages or phone calls to your smartphone from the study team. The purpose of this is to follow-up on your progress in the study, check if you have any questions, and provide you reminders regarding how to use the device. If you do not agree to receive occasional text messages and/or phone

calls from the researchers, you shall notify the clinic staff before you sign this document.

As instructed in the run-in stage, once a report is made, a baseline diary questionnaire will appear on the app, and you will be requested to record your pain intensity level, the presence/absence of aura and associated migraine symptoms (nausea, light sensitivity, sound sensitivity, and touch sensitivity) as well as your stress levels and your ability to perform usual activities. You will also be asked to answer these questions at 2 hours and 24 hours post initial report, with the addition of medication usage information.

Visit 3- Following completion of the treatment stage, you will return to the clinic in order to return your devices and fill out a questionnaire. You will enter the final stage of this study, the free-use stage.

The **free use stage** will last for 8 weeks. During this stage you will be requested to incorporate the Nerivio device into your usual care. This means you will have several treatment options at your disposal for each headache or migraine, and you will decide which is the best option for you at that time. This includes option of using treatment with Nerivio only, treatment with medication only, both treatment options, or none. As done in the previous stages, you will be asked to report all your migraines and headaches at onset, and no later than 60 minutes. This will be reported regardless if you are using the device or not. As instructed previously, once a report is made, a baseline questionnaire will appear on the app, and you will be requested to record your pain intensity level, the presence/absence of aura and associated migraine symptoms (nausea, light sensitivity, sound sensitivity, and touch sensitivity) as well as your stress levels and your ability to perform usual activities. You will also be asked to answer these questions at 2 hours and 24 hours post initial report, with the addition of medication usage information.

Visit 4- Following completion of the free-use stage, you will return to the clinic in order to return your devices and fill out a questionnaire. You may return your devices by mail instead of returning to the clinic, without any cost to you. Please ask the site staff for instructions on how to return the devices.

The table below outlines what you will be responsible for during the course of this study.

Schedule	What you do
<p>Enrollment Visit 1 (Day 0)</p>	<ul style="list-style-type: none"> • Arrive to _____ for your scheduled appointment. • Bring packages of any medications you are taking (for any medical condition). • Bring packages of any migraine rescue medications you are taking if you experience a migraine attack. • Meet with Dr. _____, or his physician designee and the study team to answer questions about your general health and your migraines. • If receiving this form today, take the time to read it carefully and make sure all your questions and concerns are answered. • You may request another appointment in case you would like to read this form at home and consult with family members or friends.

	<ul style="list-style-type: none"> • If you are a female of child-bearing potential, you will provide a urine sample for a pregnancy test. • If agreeing to participate in the study your medical and migraine information will be collected by the study team. • You will be asked to complete a questionnaire regarding your migraine and quality of life • A member of the study staff will download the smartphone application to your mobile phone. • Receive explanation on how to operate the smartphone application. • Receive explanation on how to operate the Nerivio device. • Receive explanation on how to complete your migraine diary.
<p>Run-in-stage Duration of 4 weeks</p>	<ul style="list-style-type: none"> • Complete the diary whenever you experience a migraine or headache. • At the end of this month you will be contacted via telephone by a member of the study staff to schedule your next visit
<p>Visit 2</p>	<ul style="list-style-type: none"> • We will train you in detail on how to use of the device. • Ask us any questions. • Take the Nerivio device home with you
<p>Treatment Phase Duration of 4 weeks</p>	<ul style="list-style-type: none"> • Always have the device and your smartphone available. • Use the device for the treatment of all migraine and headache onset (and always with 60 minutes of onset). • To comply, you: <ul style="list-style-type: none"> ▪ avoid taking rescue medication for 2 hours from treatment start. ▪ report the 2-hour and the 24- hour post treatment feedback through the smartphone application • The application will ask you to rate your migraine pain level at the beginning of the treatment, after 2 hours, and after 24 hours post treatment on a scale of 0-3 (0= no pain; 1= mild; 2= moderate; 3= severe) • Call the study team if there is any change in your medical condition. • At the end of this phase, you will be contacted by a member of the study team to schedule your next visit.
<p>Visit 3</p>	<ul style="list-style-type: none"> • Arrive to _____ for your scheduled appointment. • Return the used Nerivio devices. • Meet with Dr. _____ or his physician designee and the study staff to answer questions about your general health and your migraines. • Complete an end of treatment questionnaire. • We will provide you with additional devices for the free-use stage during this visit.
<p>Free use stage Duration of 8</p>	<ul style="list-style-type: none"> • Treat all your migraines and headaches as preferred, and report using the smartphone app questionnaires at 0, 2, and 24 hours post treatment. • At the end of this period, you will receive a call from a research team

weeks	member to schedule your end of study visit or receive instructions on how to return the devices.
Study Exit (Visit 4)	<ul style="list-style-type: none"> • Arrive to _____ for your scheduled appointment. • Return the Nerivio device. • Complete an end-of-study questionnaire.

What are the risks and possible discomforts?

You may have side effects while participating in this study. The device used in this study may cause temporary mild side effects that should resolve shortly after the treatment.

The side effects that were reported in previous studies include:

- warmth sensation,
- redness,
- numbness of the hand/arm,
- pain in the arm,
- itching
- tingling
- Muscle spasms

All the side effects were mild and solved after the treatment without any need for medical interventions

You should talk to your study doctor about any side effects experienced while taking part in the study.

You should not become pregnant while participating in this study. The potential effects of the Nerivio device on an unborn baby have not been assessed. Women should not breastfeed while on this study. It is important to understand that you need to use birth control while on this study.

If you think you might be pregnant or your partner thinks that she might be pregnant, contact Dr. _____, at (XXX) XXX-XXXX.

The Nerivio device was proven to be a safe technology, therefore the study is expected to have a minimal risk profile.

For more information about risks and side effects, ask your study doctor.

How will I find out about new information?

We will tell you about any new information that may affect your health, welfare or change your decision to be in this study.

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.

What are the possible benefits?

We cannot promise any benefits to you or others from your taking part in this research. However, you may experience less migraine pain and other symptoms without having to take rescue medications to treat your attacks in the course of the study. Alternatively, you may experience partial improvement. Another benefit is possibly learning more about your medical condition during the course of the study.

Last, information gained from this research could lead Nerivio to help others with chronic migraine in the future.

What are my alternatives?

Please talk to your doctor about your choices before deciding if you will take part in this study. Your alternatives include pain relieve medications and preventative treatments, physical therapy, nerve blocks, Botox, or the use of other nerve stimulators.

Are there any additional costs?

You will not incur any additional costs by participating in this study. The study device will be provided at no charge to you by the study sponsor. You will not be charged for any study-related activities, including study visits.

Will I be paid?

If you agree to take part in this research study, you will be paid \$50 for each visit after you complete all study visits.

If I do not want to take part in the research study, are there other choices?

Instead of being in this research study, your choices may include approved medications for migraine.

You do not have to participate in this study to be treated for migraine.

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

How will information about me be kept confidential?

Federal regulations give you certain rights related to your health information. The study doctor must get your authorization (permission) to use or give out any health information that might identify you.

If you have questions about your privacy rights, please call the Western Institutional Review Board® (WIRB®) at 1-800-562-4789 or 360-252-2500.

What information may be used and given to others?

Information that identifies or can be used to identify you such as your address, where you work, your date of birth, your social security number, your health information and other similar personal information may be collected for this study.

Your health information that may be used for this study and given to others can be in different forms and may include:

- Written information, such as what is in your medical chart, or the record of your study visits
- Electronic information, which is information stored in computer systems, such as billing data
- Verbal information, such as in phone calls made as part of this research study
- Information obtained during this research about
 - Past and Present Medical History
 - Physical exams
 - Laboratory, x-ray, and other test results
 - Diaries and questionnaires
 - The diagnosis and treatment of a mental health condition
 - Study procedures, treatments and follow-up
- Records about the study device

Your Social Security number will be collected and used to process any payment for participation you may receive.

Who will be able to use your health information and give it to others?

Information about your health may be used and given to others by the study doctor and his/her study team. They will see the research information during and after the study.

Who will be able to get your health information and how and why will they use it?

Study records that identify you will be kept private. You will not be identified in study records or publications disclosed outside _____, except as detailed below.

Investigators will share information collected from this research study with:

- study sponsor and/or its agents,
- other researchers,
- accrediting agencies,
- data safety monitoring board,
- clinical staff not involved in the study who may be involved in participant's treatment,
- health insurers or payers

The following reviewers may access your study and medical records to make sure that this study is being done properly:

- Representatives from federal and state government oversight agencies such as the Food and Drug Administration, National Institute of Health, etc.
- Representatives from the study sponsor
- Representatives from _____ Human Research Protection Program (the group of people that oversee research at this institution)

We will do our best to protect the privacy of your records, but it is possible that once information is shared with people listed on this form, it may be released to others. If this happens, your information may no longer be protected by the federal law.

In the future, we may publish results of this study in scientific journals and may present it at scientific meetings. If we do, we will not identify you.

If the researchers learn about potential serious harm to you or someone else or other public health concerns, it will be shared with the appropriate authorities.

What if I decide not to give permission to use and give out my health information?

By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to be in this research.

May I review or copy the information obtained from me or created about me?

You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?

If you change your mind about being in the study, you may withdraw at any time. If you want us to stop collecting your health information, you need to send a letter to the researcher at the address on page one of this consent form.

Your letter needs to say that you have changed your mind and do not want the researcher to collect and share your health information. You may also need to leave the research study if we cannot collect any more health information. We may still use the information

we have already collected. We need to know what happens to everyone who starts a research study, not just those people who stay in it.

When will the research end and when will my health information no longer be used?

This permission will be good until the end of the research study.

Will I be able to see my research records?

You will not be allowed access to your research records during the course of the research, but you will be allowed access to your research records once the research is complete.

Can anyone remove me from the study?

You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He will tell you how to stop your participation safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from Nerivio can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

The study doctor or the sponsor can remove you from the research study at any time without your approval. Possible reasons for removal include:

- the study doctor thinks it is necessary for your health or safety;
- you have not followed study instructions;
- the sponsor has stopped the study; or
- administrative reasons require your withdrawal.

The sponsor can also end the research study early.

If I have a bad side effect, who will pay the doctor and hospital bills?

If you are hurt from being in this study, you will receive medical care and treatment as needed from _____. Theranica has agreed to pay for reasonable and necessary expenses incurred by you for medical care. These expenses include any and all medical, hospitalization and hospitalization related expenses caused by research procedures.

By signing this consent form, you have not given up any of your legal rights.

Who is Funding the Study?

Dr. _____ and the research study staff receive funding from Theranica to conduct this research. Theranica, the manufacturer of the investigational device being used in this study, is providing the study device at no cost to the researcher or research participant.

Involvement of the General Practitioner (GP)/family doctor

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Lead Principal Investigator: Dr. TBD, MD

Study title: An open label, single arm, multicenter study assessing the efficacy and safety of Nerivio, a remote electrical neuromodulation device, for acute treatment of migraine in people with chronic migraine

With your consent, your GP will be informed of your involvement in the study. Any other medical practitioners who treat you (for example should you be admitted to the hospital for any reason) may also be informed.

If I have any questions or problems, whom can I call?

If you have any questions, concerns, or complaints about the research study now or later, or if you think you have been injured by the research, contact the study doctor, _____, MD, or an associate at (XXX) XXX-XXXX, or at (XXX) XXX-XXXX (24 Hours).

If you cannot reach the study doctor, you may call the _____ Clinical Trials Office at (XXX) XXX-7XXXX.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems, questions, complaints, or concerns you may have about the study, please contact the office of the Institutional Review Board at:

_____ Institutional Review Board

Address:

Telephone:

E-mail:

WIRB is a group of people who perform independent review of research.

WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WIRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

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SIGNATURE PAGE

Printed Name of Study Participant

Street: _____

City: _____ State: _____ Zip: _____

CONSENT SIGNATURE

For study participants:

Participant's Signature

Date

Witness's Printed Name

Witness's Signature

Date

Name of Person Conducting
Informed Consent Discussion

Role in the study

Signature

Date

----- Use the following only if applicable -----

If this consent form is read to the participant because the participant is unable to read the form, an impartial witness not affiliated with the research or investigator must be present for the consent and sign the following statement:

I confirm that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the participant. The participant freely consented to be in the research study.

Signature of Impartial Witness

Date

Note: This signature block cannot be used for translations into another language. A translated consent form is necessary for enrolling participants who do not speak English.