RESEARCH PARTICIPANT INFORMATION AND CONSENT FORM

Site:
Address:

TITLE: A Randomized, Double Blinded, Sham controlled Clinical Study to Evaluate the Safety and Efficacy of the Nerivio Migra 1, a Neuromodulation Device, for the acute treatment of Migraine

PROTOCOL NO.: TCH-003
NCT03361423

SPONSOR: Theranica Bio-Electronics Ltd.

INVESTIGATOR: XXXXXXXXXXX

STUDY-RELATED PHONE NUMBER(S):

You are being asked to take part in this study because you suffer from migraine.

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

The purpose of this study is to compare the effects of an investigational device called the Nerivio Migra 1 device with the effects of a sham device on you and your migraine. "Investigational" means that the device has not been approved for general use, but is permitted to be used and studied in this research trial. In this study, you will get either an active Nerivio Migra 1 or a non-active (sham) Nerivio Migra 1.

How many people will take part in this study?

About 270 participants will be in this research study in the USA and Israel, with up to 50 participants from this site.

How long will you be in the study?

We expect that you will be in this research study for about 2 months**.** At the end of the study, you will have the option of participating in a 2-month open-label extension using the active Nerivio Migra 1, regardless to the group you were assigned during the research stage.

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?

Study participants will be divided equally between study groups (either the active Nerivio Migra 1 device group or the non-active Nerivio Migra 1 device group). Each individual will receive a device and a smartphone application (as well as a smartphone if you do not have one, or if you do not want to use your own) to control the device and to record your feedback regarding its effect on your migraine.

The Nervio Migra 1 device is intended for treatment of migraine attacks. It is a non-invasive neuromodulation device operated via a smartphone application. The device is worn on the upper arm, and treatment is self-administered at the immediate onset of a migraine attack. The device delivers a series of non-painful electrical pulses to your skin that stimulate the body to initiate endogenous pain inhibition mechanism in the brain. 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.
- If you are a female of childbearing potential, a urine sample for pregnancy test will be taken.

The study concept:

- If the exams, tests and procedures show that you are eligible to participate in the study, and you choose to take part, you will undergo the following procedures. You will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. A computer program will place you in one of the groups. Neither you nor study staff can choose the group you will be in. You will have an equal chance of being placed in either group. You will not know to which group you have been randomized.
  - **If you are in group 1, 'Active Nerivio Migra 1':** You will receive electro-stimulation with parameters being evaluated for effectiveness in treating migraine attacks.
  - **If you are in group 2, 'Sham Nerivio Migra 1':** You will receive electro-stimulation with parameters not expected to be effective for migraine treatment, to serve as means of comparison with the first group.

Study Chart and Timelines

If you agree to take part in this study, you will start at **Enrollment** (Visit 1). During the enrollment visit you we will assess your eligibility to participate in the study and you will need to sign this Informed Consent Form. Following your consent, you will be required to answer questions regarding your medical status and fill out a questionnaire regarding your migraine. You will receive training of how to operate the application and complete the migraine diary during migraine attacks.

During the **Roll-in-stage** (the first month), you will be asked to complete a diary about your migraine attacks at every attack, as if you were treated by the device. This month is a preparation period in which we will test your ability and compliance with the study requirements (operate the diary on time, report your migraine symptoms, handling the application etc….).

After the roll-in-stage, you will visit the clinic again, for **Randomization** (Visit 2). You will receive a training of how to operate the Nerivio Migra 1 device 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.

The **Treatment stage** will last the duration of treating 5 migraine attacks, or the next 1 month, whichever comes first. During that stage you will be requested to carry the Nerivio Migra 1 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 appears, and no later than 60 minutes from your migraine onset.

In addition, 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.

Following completion of the treatment stage, you will have the option to participate in an **Open label extension stage**. In the open-label stage, you will receive an active Nerivio Migra 1 device for 2 months to your personal use, regardless to the group you were assigned in the study.

When you are finished using Nerivio Migra 1:
You will return to _____, for an end of study visit.

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

Roll-in-stage

Schedule	**What you do**
Enrollment Visit 1 (Day 0)	• 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.

	• 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, a member of the study staff will download the smartphone application to your mobile phone or provide you with a mobile phone in case you do not have one. • Receive explanation on how to operate the smartphone application. • Receive explanation on how to complete your migraine diary.
Roll-in-stage (Days 1-30)	• Complete the diary whenever you experience a migraine attack. • At the end of this month you will be contacted via telephone by a member of the study staff to schedule your Randomization visit
Randomization Visit 2 (Day 31-37)	• Your compliance will be assessed, and if sufficient, you will be randomized to one of the two groups (the active treatment group or the sham treatment group). • We will train you in detail regarding use of the device. • Ask us any questions. • Take the Nerivio Migra 1 home with you.

Treatment stage

Schedule	**What you do**

Treatment stage
 	
Duration of **5 migraine attacks**, or 1 month after randomization
	• Activate the Nerivio Migra 1 Smartphone application and device whenever you have a qualifying migraine attack.
	  ○ A qualifying migraine attack:
	  ▪ Occurs after at least 48 consecutive hours of headache freedom
	  ▪ Is treated with Nerivio Migra 1 within 60 minutes post migraine onset
	  ▪ Is treated for at least 30 continuous minutes with the Nerivio Migra 1
	  ○ To be in compliance, you:
	  ▪ Must not have taken rescue medications within 4 hours prior to this migraine
	  ▪ Cannot take rescue medication for 2 hours after Nerivio Migra 1 treatment
	  ▪ Must submit the 2-hour post treatment feedback through the smartphone application
	
	• Rate your migraine pain level at the beginning of the treatment, after two hours, and after 48 hours post treatment on a scale of 0-3 (0= no pain; 1= mild; 2= moderate; 3= severe)
	• Call Dr. _____, his physician designee or the study staff

	if there is any change in your medical condition. • At the end of the month, you will receive a call from a member of the study team to schedule your study exit visit.
Study Exit (Visit 3)	• Arrive to _____ for your scheduled appointment. • Return the Nerivio Migra 1 device and the study smartphone, if received. • Meet with Dr. _____ or his physician designee and the study staff to answer questions about your general health and your migraines. • Indicate whether you are interested in the open-label extension stage. If you are interested, we will provide you the device for the open label extension stage during this visit. If you are not interest. This will be your end-of-study visit

Open-label extension stage

Schedule	What you do
Open label visit	• Meet with Dr. _____, or his physician designee and the study team to answer questions about any change in your general health and your migraines. • You will receive a device and a study smartphone for 2 months
2 month Open-label extension period	• Treat all qualifying migraines as above, and report migraine pain using smartphone app at 0, 2, and 48 hours post treatment, as above. • At the end of this period, you will receive a call from a research team member to schedule your end of study visit.
End of open label visit	• Arrive to _____ for your scheduled appointment. • Return the Nerivio Migra 1 device and the study smartphone, if received. Meet with Dr. _____ or his physician designee to answer questions about your general health and your migraines.

What are the risks and possible discomforts?

You may have side effects while participating in this study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects are anticipated to be rare and may be mild or moderate. Your health care team may give you medicines to help lessen side effects, as needed. Many side effects go away soon after you remove the Nerivio Migra 1. In some cases, side effects may never go away.

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

In a previous study, 86 participants were treated with the same device. No adverse events related to the device or treatment were reported.

Adverse events that were previously reported with other similar transcutaneous electrical nerve (TENS) devices included:

Likely

- Minor skin irritation from wearing the device, which disappears shortly after the treatment is over

Less Likely

- Red marks at the site of stimulation that fade shortly after the treatment is over.
- Sensation of warmth where the device touches the skin. This disappears shortly after the treatment is over.
- A sensation of itching, tingling or stinging at the site of stimulation which fades after treatment.
- Slight muscle fatigue or weakness in the arm where the device was applied. This should go away shortly after treatment.

Very unlikely

- Slight muscle spasms in the arm where the device was applied. This should go away shortly after treatment.

You should not become pregnant while participating in this study. The potential effects of the Nerivio Migra 1 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. Check with the study staff about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study.

If you think you might be pregnant or your partner thinks that she might be pregnant, contact Dr. _____, at (XXX) XXX-XXXX.
Experimental treatments may have side effects that no one knows about yet. The Nerivio Migra 1 device is based on a well-known and safe technology, and 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.

Additionally, patients will be closely observed by the study staff throughout their participation in the study.

Last, information gained from this research could lead Nerivio Migra 1 to help others 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 acute medications for each attack, chronic medications to try to prevent attacks, physical therapy, nerve blocks, 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 $100.00 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 the Nerivio Migra 1can 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

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.

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.