# REMOTE ELECTRICAL NEUROMODULATION FOR ACUTE TREATMENT OF MIGRAINE IN PEOPLE WITH CHRONIC MIGRAINE: A POOLED ANALYSIS OF EFFICACY AND SAFETY

Grosberg B[1], Lin T[2], Vizel M[2], Schim J[3], O'Carroll C[4], Nierenburg H[5], Wright P[5]

[1]Hartford Healthcare Headache Center, CT, USA; [2]Theranica Bio-Electronics LTD., Netanya, Israel; [3]The Neurology Center of Southern California, Carlsbad, CA, USA;

[4]Hoag Neuroscience Institute, CA, USA; [5]Nuvance Health, Poughkeepsie, NY, USA

## Background

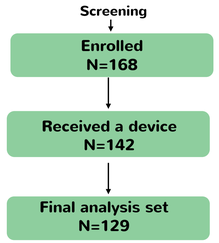
Remote electrical neuromodulation (REN) is an acute treatment of migraine which stimulates upper arm peripheral nerves to induce conditioned pain modulation (CPM)[1]. The safety and efficacy of REN have been previously assessed for migraine in a randomized, double-blind, sham-controlled multi-center study conducted on people with episodic migraine[2]. The current analysis reports on pooled efficacy and safety data from a pilot study[3] and a larger main study in chronic migraine. Both trials enrolled similar patient populations and were subject to similar design, methodology requirements, and endpoints, allowing the pooling of data for analysis.

The REN device (Nerivio®), Theranica Bio-Electronics Ltd., Israel) is a wireless wearable battery-operated stimulation unit controlled by a smartphone software application. The device is applied to the upper arm and produces a proprietary electrical signal comprising a modulated symmetrical quad-phasic square pulse with a modulated frequency of 100-120-Hz, pulse width of 400 µs, and up to 40 mA output current (adjusted by the user).

## Methods

### Participants

Patients were adults aged 18–75 years who met the ICHD-3 criteria for chronic migraine. Both trials were open-label, single-arm studies in people with chronic migraine, and included a 4-week treatment phase in which they were asked to treat their headaches with the device. Pain severity levels, associated symptoms and functional disability were recorded at treatment initiation, 2- and 24-hours post-treatment.




### Outcomes

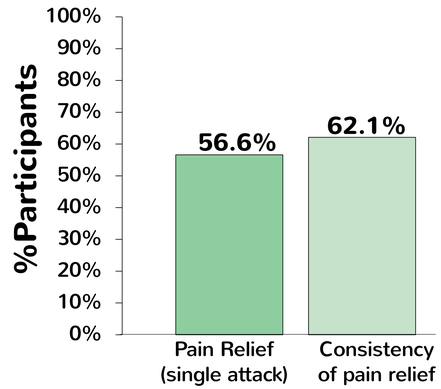
Efficacy endpoints included pain relief, pain-free, disappearance of associated symptoms, and improvement in function at 2 hours post-treatment. Sustained pain responses at 24 hours and within-subjects consistency were also assessed.

### Data analysis

The first reported treatment was considered a training treatment and was only included in the safety analyses. The efficacy evaluation was based on the first treated headache with baseline and 2 hours assessment following the training treatment (hereby termed test treatment).

## Results

The incidence of device-related adverse events was low (1.4%).




| Endpoint | Result |
|---|---|
| Pain relief at 2 hours | 56.6% (73/129) |
| Pain freedom at 2 hours | 22.5% (29/129) |
| Disappearance of nausea/vomiting at 2 hours | 51.7% (30/58) |
| Disappearance of photophobia at 2 hours | 39.8% (39/98) |
| Disappearance of phonophobia at 2 hours | 45.7% (37/81) |
| Sustained pain relief at 24 hours | 75.4% (43/57) |
| Improvement in functional ability at 2 hours | 53.2% (33/62) |
| Improvement in functional ability at 24 hours | 63.9% (23/36) |
| Within-subject consistency of pain relief | 62.1% (80/129) |

## Conclusions

- REN provides clinically meaningful relief of migraine pain and associated symptoms in people with chronic migraine
- Most participants who used REN achieved pain relief at 2 hours post-treatment in most of their treated attacks
- REN is well tolerated and safe
- REN may provide an alternative acute therapy in patients with chronic migraine, holding the potential to reduce medication use in a population with increased risk of developing medication overuse headache

**References**

1. Nir and Yarnitsky, *Current opinion in supportive and palliative care,* 2015
2. Yarnitsky, et al., *Headache*, 2019;
3. Nierenburg at al., *Pain and Therapy*, 2020

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www.theranica.com
info@theranica.com