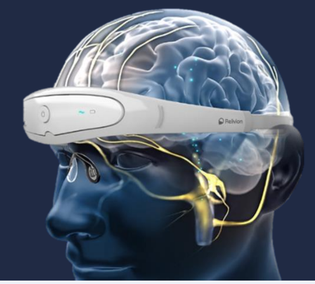
Initial Efficacy Evidence of Migraine Preventive Treatment Using External Combined Occipital and Trigeminal Nerve Stimulation

Roni Sharon, MD[1,2] and Stewart Tepper MD[3]

1 Sheba Medical Center, Ramat-Gan, Israel. 2 Sackler School of Medicine, University of Tel Aviv, Tel Aviv, Israel. 3 Geisel School of Medicine at Dartmouth, Hanover, NH, USA; Dartmouth Headache Center, Lebanon, NH, USA.



Neurolief Brain Innovation

STUDY OBJECTIVE

- The current retrospective study was designed to collect real-world data regarding the safety and efficacy of Relivion®, a combined occipital and trigeminal neuromodulation system (COT-NS) in preventive treatment of migraine in high frequency and chronic migraine patients.

BACKGROUND

- Preventive migraine treatment is recommended for patients who have frequent or disabling migraine attacks.
- Many migraine patients on traditional oral preventive migraine treatments are unable to achieve optimal efficacy or experience significant tolerability issues. Due to these factors, only 3-13% migraine patients use preventive treatments.[1]
- The anti-CGRP mAbs have a modest effect in prevention of migraine with the average placebo-subtracted 50% responder rates for reduction in migraine headaches at 21.4% in episodic migraine and 17.4% in chronic migraine.[2] According to a retrospective observational cohort study that analyzed commercial and Medicare claims, only 49% of migraine patients were >80% adherent to anti-CGRP mAb treatment over a six-month time frame .[3]
- Currently available neurostimulation treatments have mixed results as preventive treatments for migraine.
  - Remote electrical stimulation: no clinical evidence.
  - Non-invasive vagal stimulation: pivotal study did not meet clinical endpoint of reduced headache days.[4,5]
  - Transcranial magnetic stimulation: clinical evidence based on an open-label observational study.[4,5]
  - External transcutaneous supraorbital nerve stimulation: clinical evidence of reduction in headache days significantly less when compared to pooled studies of oral topiramate.[5]
  - Occipital nerve stimulation: highly invasive surgical procedure and clinical evidence is mixed.[4]
- Relivion is the first and only non-invasive brain neuromodulation technology that provides precise activation of the occipital & trigeminal neural pathways via three adaptive output channels to maximize therapeutic effect.
- Relivion is FDA cleared for the acute treatment of migraine. Clinical results from the US pivotal study (RIME) demonstrated:
  - 46% Pain Freedom at 2HRs vs 12% sham (p <0.0001)
  - 75% MBS Freedom at 2 HRs vs 47% sham (p= 0.0099)
  - 60% Pain Relief at 2HRs vs 37% sham (p=0.018)
  - 47% Freedom from all Migraine Symptoms at 2HRs vs 11% sham (p= 0.0003)
- Relivion is not yet cleared for the prevention of migraine.

OUTCOME METHODS

- Twenty-one patients with **high-frequency episodic migraine** or **chronic migraine**, self-administered 20-minute treatments 5-7 days a week with the COT-NS system (Relivion®) and electronically reported migraine characteristics for a duration of 3 months.
- **Primary efficacy measure:** change (%) in monthly Headache days in the 3rd treatment month compared to baseline.
- **Responder-rate measure:** patients with ≥50% reduction in monthly headache days.
- **Safety measure:** Adverse events were collected.

Demographics	Migraine Patients N=21
Gender- Female (%)	86%
Average Age (Min, Max)	39 (24,4)
Migraine Characteristics	
Baseline Average Headache Days	14.6
Chronic Migraine (%)	57%
High Frequency Episodic Migraine (%)	43%
Migraine with Aura (%)	19%
Menstrual Migraine (%)	14%

RESULTS

Reduction in Headache Frequency

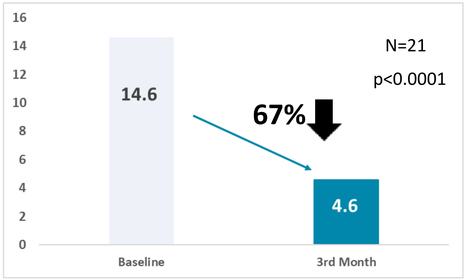


Figure 1: Reduction in Average Headache Days

Responder Analysis

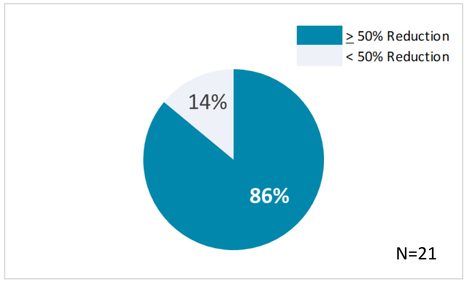


Figure 2: % of Patients with ≥50% Reduction in Monthly Headache Days

RESULTS

Individual Responder Analysis

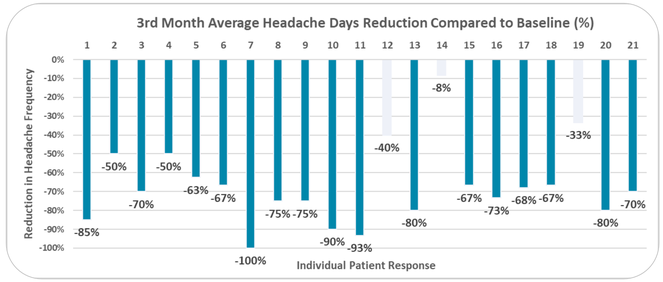


Figure 3: Individual Reduction of Monthly Headache Days at 3 Months

SAFETY ANALYSIS

- Relivion demonstrated a very favorable tolerability profile in this retrospective study.
- One case of minor skin irritation was reported and resolved within 48 hours.

CONCLUSIONS

- These are retrospective analyses evaluating the real-world data on the efficacy of Relivion in the preventive treatment of migraine.
- **67% reduction in average monthly headache days from baseline to final treatment month.**
- **86% of patients reported a ≥50% reduction in monthly headache days from baseline to 3rd month.**
- **Relivion was well tolerated with minimal adverse events.**
- Based on these findings, Relivion was highly effective in reducing monthly headache days in a difficult-to-treat migraine population.
- A larger scale, double blind, sham-controlled study is needed to further establish these promising clinical results.

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1.American Headache Society (2018). The American Headache Society Position Statement On Integrating New Migraine Treatments Into Clinical Practice. Headache; The Journal of Headache and Facial Pain. https://doi.org/10.1111/head.13456. (Headache 2019; 59:1-18) 2.Schoenen J, et al. Monoclonal antibodies blocking CGRP transmission: An update on their added value in migraine prevention. Rev Neurol (Paris). 2020 Dec;176(10):788-803. 10.1016/j.neurol.2020.04.027. Epub 2020 Aug 2. PMID: 32758365. 3.Foster S, et al. Adherence and Persistence Associated with Calcitonin Gene-Related Peptide (CGRP) Monoclonal Antibodies (mAbs) Compared to Non-CGRP mAb Treatments for Prevention of Migraine. Poster presented at the American Headache Society Virtual Annual Meeting; June 2021. 4.Halker-Singh R, et al. Neuromodulation for the Acute and Preventive Therapy of Migraine and Cluster Headache. Headache; The Journal of Headache and Facial Pain. (2019; 59:33-49) 5.Miller S, et al. Neurostimulation in the treatment of primary headaches. Pract Neurol 2016; 16:362–375.