

PRESTO CLINICAL TRIAL OVERVIEW

gammaCore™ : A Promising, New Non-Drug Treatment Option for Migraine

The PRospectivE Study of nVNS for the Acute Treatment Of Migraine: PRESTO

About PRESTO:

PRESTO is a prospective multi-center, randomized, double-blind, sham-controlled study of gammaCore, a non-invasive vagus nerve stimulator, for the acute treatment of migraine. Subgroup analyses from this trial supports the FDA clearance for an expanded label for gammaCore in the acute treatment of pain associated with migraine in adult patients.

Trial Design:

Treatment Highlights:

- Bilateral treatment within 20 minutes of onset of pain; retreat 20 minutes after the start of Treatment 1 if pain persists
- Option to retreat 2 hours after the start of Treatment 1 if pain has not improved
- Subjects were asked to withhold rescue medication for at least 2 hours

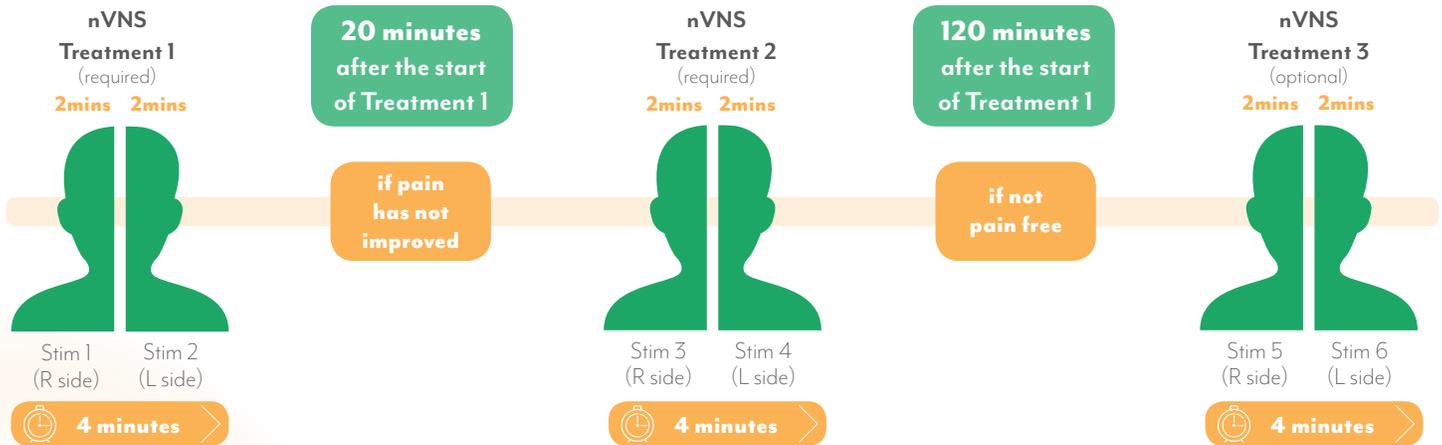
Trial Periods:

- **Period 1:** Observational Period (4 weeks)
- **Period 2:** Double-blind Period (4 weeks or until 5 attacks were treated)
- **Period 3:** Open-label Period (4 weeks or until 5 attacks were treated)

Inclusion Criteria:

- Adults aged 18 to 75 years diagnosed with migraine (according to *The International Classification of Headache Disorders criteria*)
- 3-8 migraine attacks per month and fewer than 15 headache days per month

Stimulation Protocol:



Study Endpoints:

Efficacy

Primary Endpoint

Pain free (and no rescue medication) at 120 minutes post-treatment for Randomized Period, Attack 1

Select Secondary Endpoints

Mild or no pain at 30, 60, and 120 minutes

Consistency of response at 120 minutes, calculating $\geq 50\%$ responder rates, for both pain freedom and mild or no pain in those with ≥ 2 treated migraine (post-hoc)

Safety and Tolerability

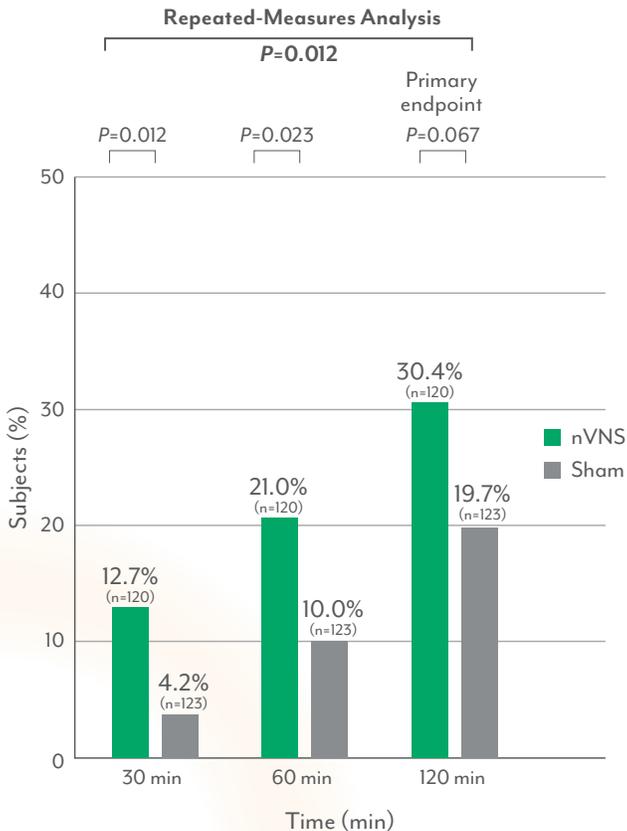
Frequency and intensity of adverse events (AEs), including determination of device relatedness

Participants:

A total of 243 patients with migraine were randomized to receive either gammaCore (N=120) or sham (N=123).

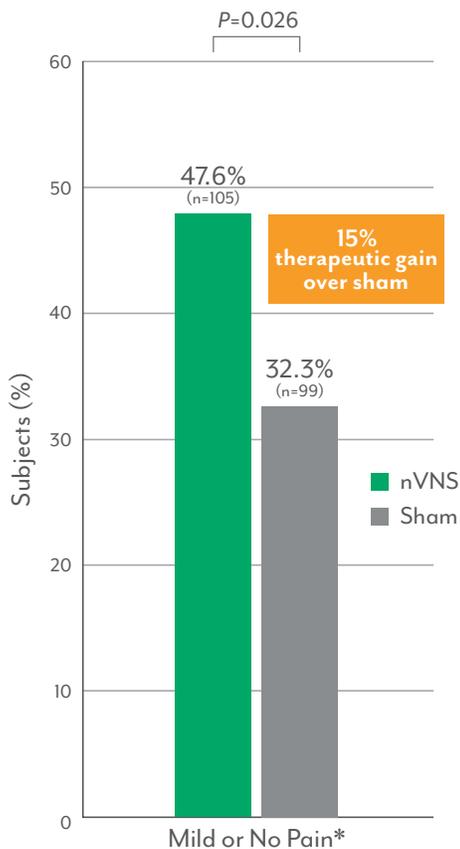
Primary Endpoint Results:

Percentage of Patients Who Were Pain-Free for the First Migraine



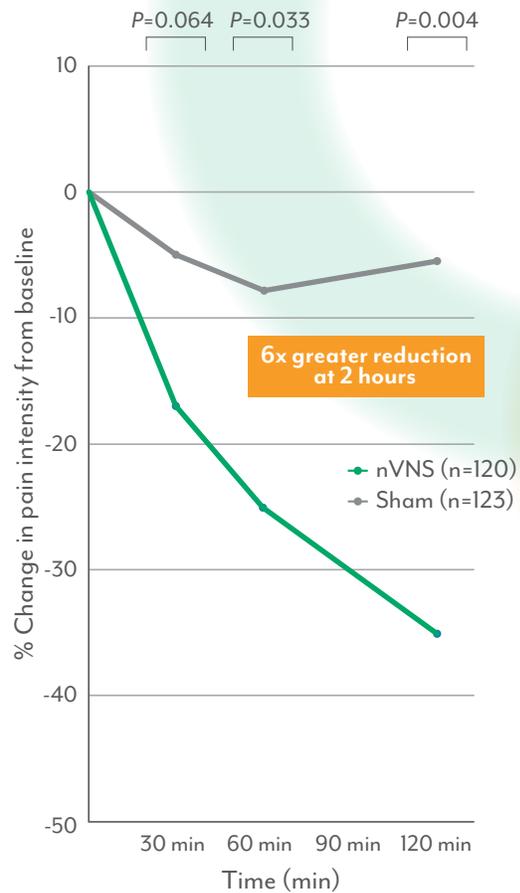
Secondary Endpoint Results:

Migraine Patients Successfully Treated $\geq 50\%$ of Migraines



*Patients with mild pain at both baseline and 120 minutes were not considered responders.

Reduction of Pain Intensity of First Treated Migraine*



*Post-hoc analysis.

Safety Findings:

As seen in other published studies, gammaCore was again found to be safe and well-tolerated, as demonstrated by a low incidence of adverse events. The majority of AEs were mild and transient, occurring during the time of active treatment. No SAEs or study discontinuations due to AEs occurred in the gammaCore group. AEs occurred in 5 patients (n=122 / 4.1%) using the gammaCore device and 16 patients (n=126 / 12.7%) using the sham device.

Important Safety Information

gammaCore (non-invasive vagus nerve stimulator) is indicated for the acute treatment of pain associated with episodic cluster headache and migraine headache in adult patients.

- The safety and effectiveness of gammaCore (nVNS) have not been established in the acute treatment of chronic cluster headache.
- gammaCore has not been shown to be effective for the prophylactic treatment of chronic or episodic cluster headache or migraine headache.
- The long-term effects of the chronic use of gammaCore have not been evaluated.
- Safety and efficacy of gammaCore have not been evaluated in the following patients, and therefore it is NOT indicated for:
 - Patients with an active implantable medical device, such as a pacemaker, hearing aid implant, or any implanted electronic device
 - Patients diagnosed with narrowing of the arteries (carotid atherosclerosis)
 - Patients who have had surgery to cut the vagus nerve in the neck (cervical vagotomy)
 - Pediatric patients
 - Pregnant women
 - Patients with clinically significant hypertension, hypotension, bradycardia, or tachycardia
- Patients should not use gammaCore if they:
 - Have a metallic device such as a stent, bone plate, or bone screw implanted at or near their neck
 - Are using another device at the same time (e.g., TENS Unit, muscle stimulator) or any portable electronic device (e.g., mobile phone)

Note: This list is not all inclusive. Please refer to the gammaCore **Instructions for Use** for all of the important warnings and precautions before using or prescribing this product.

gammaCore is available by prescription only. U.S. Federal Law restricts this device to sale by or on the order of a licensed healthcare provider.

1. Tassorelli C, Liebler E. The PRospectivE Study of nVNS for the Acute Treatment Of Migraine (PRESTO): A Sham-controlled, Double-blind, Randomised Study. Oral presentation at: Congress of the International Headache Society. September 2017. Vancouver, CA.