Rationale, Study Design, and Clinical Outcomes for the SENZA-RCT: A Prospective Comparison of HF10 Therapy and Low-frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain


Introduction

For over four decades, the primary focus of innovation in spinal cord stimulation (SCS) has been to improve the reliability of overlapping paresthesias with the distribution of chronic pain. As such, innovation has been focused on this goal:

- Multiple contacts
- Multiple leads, surgical leads
- Implantable generators
- Current vs. voltage control
- Programming algorithms
- Independent current control of electrodes
- Percutaneous placement of surgical style leads
- Accelerometer for postural adaptation

Given that HF10™ therapy (including high frequency SCS at 10 kHz) does not generate paresthesias, the focus has now shifted to clinical evidence. As such, the rationale for the approach of evaluating 10 kHz therapy in a pivotal study is presented, along with key clinical outcomes.

Methods

The objective of the SENZA-RCT study was to demonstrate a reasonable level of assurance of safety and effectiveness of the device system that delivers HF10 therapy (the Senza® System, Nevro Corp., Menlo Park, CA) in support of a pre-market approval (PMA) application to the FDA. In order to support this objective, study design input was obtained from United States regulatory agencies, clinical trial and pain management experts, as well as guidance from peer-reviewed literature. Consecutive recruitment occurred subsequent to IDE and IRB approvals. Results were compared with published, prospective, peer-reviewed, SCS studies with ≥6 months outcomes.

Given prior approvals for and common clinical usage of traditional low-frequency SCS systems, all study design inputs pointed to a pragmatic comparative trial between investigational HF10 therapy and standard SCS.

From a regulatory perspective, three SCS device systems (delivering 2-1200 Hz stimulation have received PMA approval and are clinically utilized to treat chronic intractable pain. A non-inferiority demonstration of safety and effectiveness was required for a new market entry. Therefore, a parallel arm RCT was designed to demonstrate non-inferiority of the HF10 therapy device to a traditional low-frequency SCS system.

The literature also supports such a comparative study when a standard therapy exists. Moreover, it complies with payers preference for comparative effectiveness research (active control instead of placebo control), and has direct clinical utility.

198 subjects were randomized to a treatment group across 10 comprehensive pain treatment centers. 171 passed a temporary trial and were implanted with an SCS system. Upon completion of 12-month follow-up, the observed responder rate for HF10 therapy was higher than for traditional SCS for both back and leg pain (<p<0.001, Figure 1). Additionally, the average degree of relief from back and leg pain was much greater for HF10 therapy than traditional SCS (<p<0.001, Figure 2).

Results

Figure 1. Responder rates for back and leg pain. Between group p-value <0.001 at all endpoints.

Figure 2. Longitudinal back and leg pain scores and pain relief from baseline. P<0.001 for all comparisons by repeated measures analysis of variance.

Figure 3. Comparison of HF10 therapy results in the SENZA-RCT study to published European multicenter results.

Conclusions

The SENZA-RCT study is the first randomized controlled pivotal trial in SCS history and the first to directly compare SCS technologies. This level-1 evidence with 12-month follow-up meets today’s rigorous standards for evidence-based healthcare and complies with regulatory agency and payer preference for comparative effectiveness.

References


The Senza System is an investigational device in the U.S. The SENZA-RCT study was supported by Nevro Corp.