10 kHz Spinal Cord Stimulation for Treatment of Painful Diabetic Neuropathy – A Multicenter Randomized Controlled Trial

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INTRODUCTION

Globally, 422 million people are living with diabetes[1] and approximately 20% will develop painful diabetic neuropathy (PDN),[2] a progressive chronic pain condition that significantly impacts patients' health-related quality of life. Neither pharmacological treatments nor low-frequency spinal cord stimulation (SCS) has provided significant, long-term relief for many PDN patients;[3-6] however, preliminary observational data suggest 10 kHz SCS may relieve pain and improve sensation in patients with refractory symptoms.[7]

AIM

Prospective, multicenter, randomized controlled trial (SENZA-PDN) to document the impact of 10 kHz SCS on PDN.

METHODS

Key inclusion criteria:

- PDN symptoms ≥12 months, refractory to pain medications
- lower limb pain ≥5 cm (on a 0-10 cm visual analog scale [VAS])
- appropriate for SCS

Key exclusion criteria:

- hemoglobin A1c >10%
- daily opioids >120 MMEs
- upper limb pain ≥3 cm

Randomized 1:1 to 10 kHz SCS (**Fig 1**, Nevro Corp.) vs conventional medical management (CMM)

Outcomes: pain, neurological function, quality of life

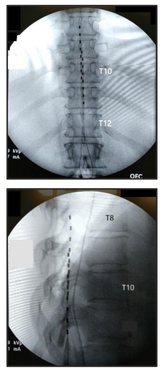

Figure 1: AP (top) and lateral (bottom) images of SCS electrodes placed epidurally along T8-T11 vertebrae.

RESULTS

Randomization and safety:

- 113 subjects randomized to 10 kHz SCS+CMM vs 103 to CMM alone
- Study arms well-matched for baseline characteristics
- No reported study-related adverse events (AEs) for the CMM group and 16 study-related AEs reported in the 10 kHz SCS+CMM group
  - 2 procedure-related infections in the SCS group (1.8% infection rate)

Met primary endpoint (≥50% pain relief without worsening of baseline neurological deficit) in the intention-to-treat population:

- 78.9% of 10 kHz SCS+CMM subjects
- 5.3% of CMM subjects
- $p < 0.001$

Outcomes in the per-protocol population:

- Improvements in pain **(Fig 2, 3)**, sensation **(Fig 4, 5)**, and quality of life **(Fig 6, 7)** in the 10 kHz SCS+CMM group

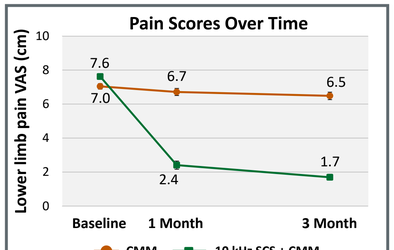

Figure 2: Average pain scores (± SEM) for CMM (n=96, orange) and 10 kHz SCS+CMM subjects (n=88, green).

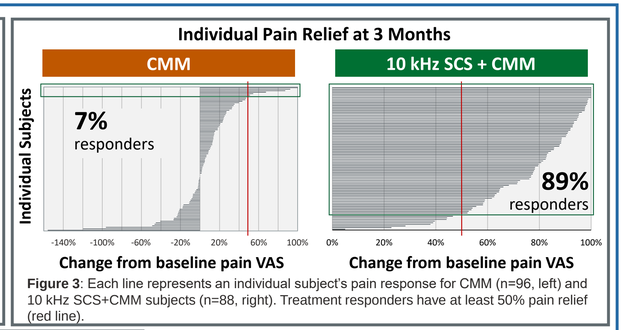

Figure 3: Each line represents an individual subject's pain response for CMM (n=96, left) and 10 kHz SCS+CMM subjects (n=88, right). Treatment responders have at least 50% pain relief (red line).

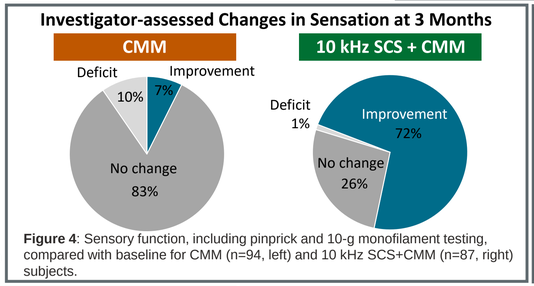

Figure 4: Sensory function, including pinprick and 10-g monofilament testing, compared with baseline for CMM (n=94, left) and 10 kHz SCS+CMM (n=87, right) subjects.

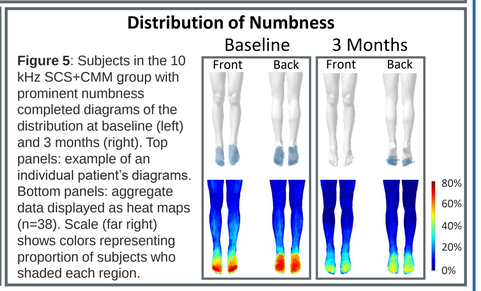

Figure 5: Subjects in the 10 kHz SCS+CMM group with prominent numbness completed diagrams of the distribution at baseline (left) and 3 months (right). Top panels: example of an individual patient's diagrams. Bottom panels: aggregate data displayed as heat maps (n=38). Scale (far right) shows colors representing proportion of subjects who shaded each region.

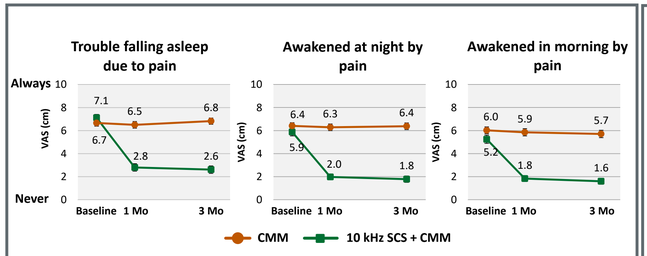

Figure 6: Average scores (± SEM) for how pain affects sleep for CMM (n=96, orange) and 10 kHz SCS+CMM subjects (n=88, green).

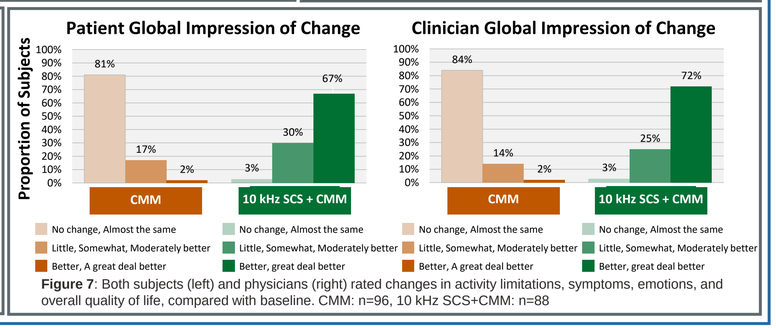

Figure 7: Both subjects (left) and physicians (right) rated changes in activity limitations, symptoms, emotions, and overall quality of life, compared with baseline. CMM: n=96, 10 kHz SCS+CMM: n=88

CONCLUSIONS

The SENZA-PDN study is the largest RCT to-date of SCS management of PDN patients and will help inform the place of 10 kHz SCS in the PDN treatment continuum. The primary endpoint was met with a significant proportion of subjects responding to 10 kHz SCS. In addition to significant pain relief, 10 kHz SCS resulted in observed improvements in sensation and quality of life measures, including reduced impact of pain on sleep. These early results are encouraging for PDN patients with symptoms refractory to the best available medical treatments. Follow-up will continue for 24 months, demonstrating whether these changes are stable over time and providing data for healthcare resource utilization analysis.

ACKNOWLEDGEMENTS

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