SPARROW™

Whitepaper

Transcutaneous Auricular Neurostimulation (tAN™) To Aid In The Reduction Of Symptoms Associated With Opioid Withdrawal

Interim Clinical Trial Results

SPARK BIOMEDICAL

We’re Dedicated to the Science

We built upon a solid history of neurostimulation therapy, then applied over 150 years of our own combined neuroscience and medical device expertise to develop a scientifically proven solution that can significantly enhance the management of opioid withdrawal. We believe in an evidence-based approach, and are committed to making ongoing investments in engineering and clinical neuroscience to advance the therapy even further — beyond opioid withdrawal.

At Spark Biomedical, we want to provide an easy, safe, and effective path forward so more patients can overcome withdrawal, heal, and achieve a better quality of life, free of opioid dependence.

Indication for Use
The Sparrow is a transcutaneous nerve field stimulator that is intended to be used in patients experiencing opioid withdrawal in conjunction with standard symptomatic medications and other therapies for opioid withdrawal symptoms under the supervision of trained clinical personnel.

Clinical Study Summary

A double blind, randomized, prospective study, including a group with delayed treatment, was designed to assess the effectiveness of the Sparrow Therapy System. The study evaluated transcutaneous nerve stimulation (tAN) as a method to aid in the reduction of symptoms associated with opioid withdrawal.

The patient population included male and female participants, aged 18-65, with a history of dependence on prescriptive or non-prescriptive opioids (n=26). Subjects were enrolled at one U.S. site based on 90% power at alpha 0.05 for detecting a mean (+SD) reduction in clinical opiate withdrawal scale (COWS) of 17 (+7) points when compared to baseline values.

In brief, study participants were randomized in a 1:1 ratio to one of two groups:

1. active transcutaneous auricular neurostimulation (tAN) + usual treatment or
2. delayed-active tAN + usual treatment

Participants in the active tAN group received tAN immediately, whereas those in the delayed-active tAN had their therapy turned on after a delay (inactive period – first 30 minutes). All participants were informed of their group assignment at the conclusion of the randomized, double blind period and all continued to receive active tAN throughout the five-day study.

Blinding

Results of the Patient Blinding Assessment showed that blinding was not able to be maintained despite adherence to all protocol procedures. This result is likely due to the initial perception of electrical stimulation during device programming, which provided a familiar sensation in line with the participant's expectation during active tAN.

Primary Effectiveness Endpoint

The primary effectiveness endpoint of this study was successful mean percent change in COWS score (defined as a ≥15% reduction) from baseline to 60 minutes after start of active tAN therapy.

Secondary Endpoint

The secondary endpoints of this study included:

- Comparison of mean percent change in COWS score in delayed active tAN versus active tAN groups at 30 minutes
- Comparison of the proportion of participants with a clinically significant reduction in COWS score (defined as a 15% or greater reduction) in delayed-active tAN versus active tAN groups at 30 minutes
- Mean percent change in COWS score from baseline to 30 minutes after start of active tAN therapy
- Mean percent change in COWS score from baseline to 120 minutes after start of active tAN therapy
- Mean percent change in COWS score from baseline to Days 2 through 5 after start of active tAN therapy

Exploratory Endpoints

The following are exploratory endpoints for this study:

- Mean change in depression symptoms measured by Patient Health Questionnaire (PHQ-9) total score from baseline to Day 5
- Mean change in PTSD symptoms measured by the PTSD Checklist for DSM-5 (PCL-5) total symptom severity score from baseline to Day 5

Safety Endpoints

Safety Endpoints included the prevalence of all adverse events (AEs), serious adverse events (SAEs), adverse device events (ADEs), serious adverse device effects (SADEs), unanticipated serious adverse device effects (USADEs), and device deficiencies.

Of the 26 subjects enrolled in the study, 14 completed the study. The study results for all subjects, including study completers and non-completers, are listed below. Data from both the active tAN and the delayed-active tAN groups were pooled for the primary effectiveness analysis. The clinical study demonstrated that the subject device met the primary endpoint.

Participant Demographics

Mean (SD) Age at Enrollment (years)	34.4 (7.2)
Mean (SD) Baseline COWS score	15.2 (2.7) Range: 9-21
Mean (SD) Duration of Opioid Use (years)	12.0 (6.7) Range: 1-27
Gender: n (n/N%)	
Female	9 (34.6%)
Male	17 (65.4%)
Race: n (n/N%)	
White	22 (84.6%)
Hispanic or Latino	3 (11.5%)
Black or African American	1 (3.8%)
Most Common Psychiatric Co-Morbidities[1]	
Depression	10 (38.5%)
Anxiety	10 (38.5%)
Bipolar Disorder	8 (30.8%)
Opioid Type[2,3]	
Heroin	23 (92.0%)
Prescription Narcotics	4 (16.0%)
Buprenorphine	1 (4.0%)
Methadone	1 (4.0%)
Mean (SD) Morphine Equivalent Daily Dose (MEDD)	1240 (677.4)

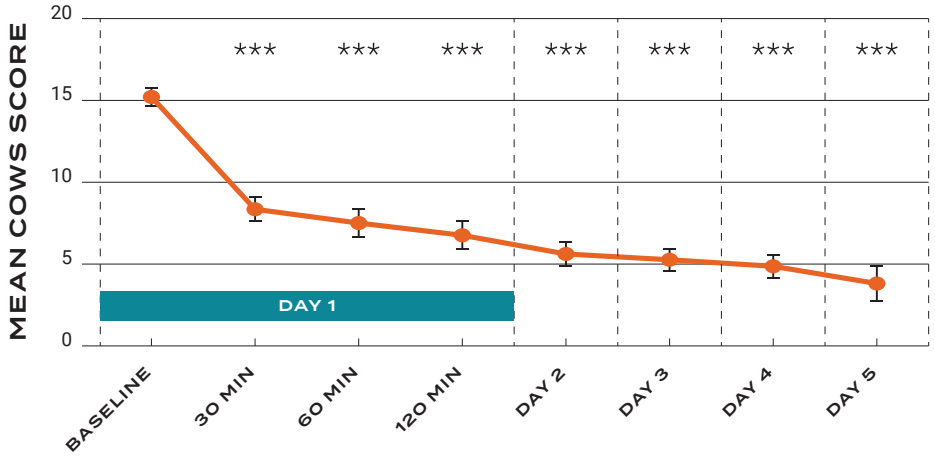
[1] Participants may have more than one co-morbidity; [2] Participants may have used more than one opioid; [3] Data not available for one participant

N=number of affected participants; N=total number of participants in group; ADHD=attention deficit hyperactivity disorder; SD=standard deviation

Primary Endpoint: Mean Reduction in COWS Score from Baseline to 60 Minutes after Start of Active tAN Therapy

Timepoint	Mean (SD) COWS Score	Mean (SD) Reduction in COWS Score	Mean (SD) Percent Reduction in COWS Score	P-Value1	95% CI	Effective Size (Cohens d)
Baseline	15.2					
60 min	7.5	7.7m (4.5)	50.4 (27.6)%	<0.005*	[41.18, Infiniity]	1.1826

*** Statistically significant difference at each time point compared to baseline (p<0.001)



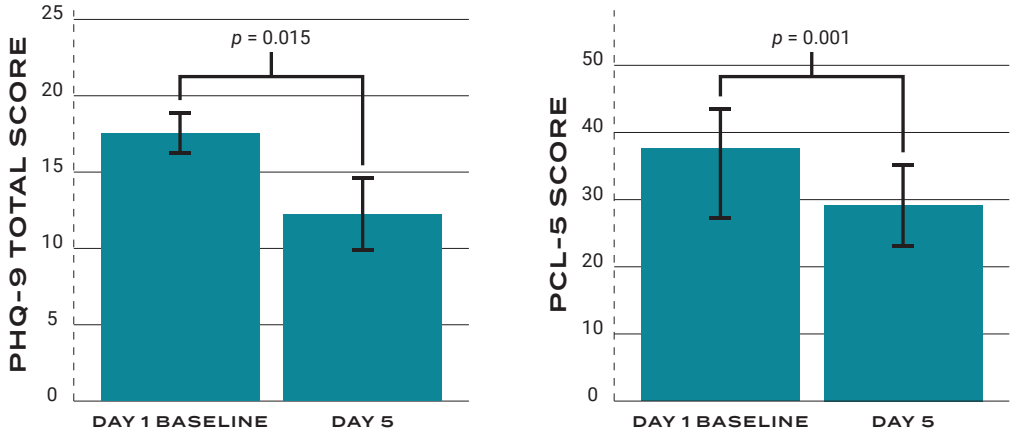
COWS Reduction Using tAN Therapy

COWS Symptom	Measurement Type (Objective vs. Subjective)	First 60 Mins (n=26)	Day 1 (n=22)
Yawning	O	85.0%	86.4%
Piloerection	O	72.7%	90.9%
Tremor	O	70.3%	76.6%
GI Upset	S/O	63.8%	77.1%
Restlessness	S/O	58.7%	80.3%
Pupil Size	O	34.2%	57.9%
Anxiety or Irritability	S	38.5%	51.9%
Runny Nose or Tearing	O	43.8%	62.5%
Sweating	S/O	47.9%	62.5%
Pulse Rate	O	44.4%	68.1%
Bone and Joint Aches	S/O	28.0%	46.0%

25% - 49% reduction 50% - 74% reduction 75%+ reduction

PHQ-9 (Depression) and PCL-5 (PTSD) Results

46.2% of participants had a clinically meaningful reduction in PHQ-9 scores at Day 5.
38.5% of participants had a clinically meaningful reduction in PCL-5 scores at Day 5.



Questionnaire (Domain)	Mean (SD) Reduction in Score from Baseline to Day 5 (N=131)	Percent Change in Score from Baseline to Day 5 (N=131)	P value	Percentage of Participants with Clinically Meaningful Reduction[1,2]
PHQ-9 (Depression)	5.4 (6.1)	31.4 (35.7)%	0.015	6/13 (46.2%)
PCL-5 (PTSD)	10.2 (9.1)	31.4 (33.4)%	0.001	5/13 (38.5%)

[1] Defined as at least a 5-point change for PHQ-9 (Kroenke K, Spitzer RL, Williams JB, et al. The Patient Health Questionnaire Somatic, Anxiety, and Depressive Symptom Scales: a systematic review. Gen Hosp Psychiatry 2010;32:345–59) and at least a 10-point change for PCL-5 (National Center for PTSD. (2016). Using the PTSD Checklist for DSM-5 (PCL-5). Retrieved from https://www.ptsd.va.gov/professional/assessment/documents/using-PCL5.pdf on June 17, 2020.

[2] Excludes one participant with score over 2 standard deviations above the mean

Safety Results

Only two device-related adverse events have occurred. Both were mild in severity and required no intervention to resolve.

Event	Device-Related	Severity	SAE	Action Taken	Outcome
Precipitated withdrawal due to naloxone challenge[1]	No	Moderate	No	Comfort medication given	Resolved without sequelae
Irregular heartbeat due to withdrawal (pre-existing, known condition)	No	Mild	No	Participant taken to ER but no treatment administered	Resolved without sequelae
Ear discomfort due to inner cymba arm[2]	Yes	Mild	No	None	Resolved without sequelae
Ear discomfort due to inner cymba arm[2]	Yes	Mild	No	None	Resolved without sequelae

[1] This event occurred in the first participant and the event categorized as the adverse event was a direct result of a naloxone challenge being administered when the participant had tested positive for opiates/morphine on Day 3.

[2] Not reported directly by participant but discovered when participant completed device usability questionnaire.

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