THERANOVA, LLC

Clinical Research Protocol

PILOT EVALUATION OF THE EMPOWER NEUROMODULATION SYSTEM IN AUD PATIENTS

NCT03983317

Protocol Number:	CRD-12-1176-01
Version Date:	December 18, 2018
Investigational Product:	Empower Neuromodulation System
IND/IDE Number:	N/A, non-significant risk study
Development Phase:	Feasibility
Sponsor:	TheraNova, LLC 101 Mississippi St. San Francisco, CA 94107
Funding Organization:	NIH-NIAAA
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Coordinating Center:	Not applicable

PROTOCOL SYNOPSIS

TITLE	Pilot evaluation of the Empower Neuromodulation System in AUD Patients
SPONSOR	TheraNova, LLC
FUNDING ORGANIZATION	NIH-NIAAA
NUMBER OF SITES	One (1)
RATIONALE	Alcohol use disorder (AUD) is a major public health concern, affecting over 16 million Americans. AUD is a highly disabling disease associated with many physical and psychiatric co-morbidities. Current AUD interventions include pharmacologic treatment and behavioral therapies; however, these are not very effective, having high rates of relapse soon after initial successful treatment. Therefore, new, more effective therapies are needed. Preclinical and clinical research has shown that stimulation of the [redacted] nerve via acupuncture can inhibit dopamine signaling in the brain's mesolimbic circuit that is responsible for drug craving and reward. While acupuncture is an excellent adjunct procedure in treatment centers, it also has limited patient acceptability as it requires patients to seek treatment in clinic. Therefore, TheraNova has developed the Empower Neuromodulation System, a portable, safe, easy-to-use neuromodulation device that stimulates the [redacted] nerve to enable a convenient and acceptable therapy to treat AUD. The overall goal of this study is to conduct a [redacted] pilot investigation into the safety, effectiveness, and usability of the Empower Neuromodulation System in AUD patients.
STUDY DESIGN	This is an open-label, pilot study.
PRIMARY OBJECTIVE	• Safety: Evaluate safety of the Empower Neuromodulation System treatment via device-related adverse events and participant-reported side effects. • Effectiveness: Evaluate the effectiveness of Empower Neuromodulation System treatment for reducing alcohol consumption (via self-reported daily consumption) over a 2-week treatment phase and compared to a pre-treatment baseline phase.

SECONDARY OBJECTIVES	The secondary study objectives are the following: • Effectiveness: Evaluate the effectiveness of the Empower Neuromodulation System treatment for reducing alcohol craving (via self-reported craving intensity (VAS responses)) over a 2-week treatment phase and compared to a pre-treatment baseline phase. • Usability: Evaluate the usability of the Empower Neuromodulation System via the System Usability Survey (SUS).
NUMBER OF PARTICIPANTS	25
PARTICIPANT SELECTION CRITERIA	Inclusion Criteria: 1. Is male or female ≥ 21 year of age at Visit 1 2. Has a current diagnosis of alcohol use disorder per DSM-5 by clinician assessment 3. Endorses Criterion 4 in DSM-5 4. Has a desire to maintain abstinence or, if not abstinent, a desire to reduce or quit alcohol use 5. Has a breath alcohol concentration of 0.00% at enrollment 6. Is able to provide informed consent 7. Is able to understand spoken and written English 8. Is capable and willing to follow all study-related procedures Exclusion Criteria: 1. Has been diagnosed with unstable psychosis, epilepsy, peripheral neuropathy, or nerve damage 2. Requires acute medical detoxification from alcohol based on a score of 12 or more on the Clinical Institute Withdrawal Assessment of Alcohol Scale (CIWA-AD) 3. Has implanted electrical and/or neurostimulator device (e.g. pacemaker, defibrillator, vagal neurostimulator, deep brain stimulator, spinal stimulator, sacral stimulator, bone growth stimulator, or cochlear implant) 4. Has an electrically conductive metal object (e.g. jewelry) that cannot be removed from the [redacted] and will directly contact the gel electrodes of the Empower Neuromodulation System 5. Will not, for the duration of the participation in the study, have a living situation that provides regular access to an electrical outlet. 6. Is pregnant, breastfeeding, or unwilling to practice birth control during participation in the study 7. Has used an investigational drug/device therapy within the past 4 weeks 8. Is deemed unsuitable for enrollment in the study by the PI

TEST PRODUCT, DOSE, AND ROUTE OF ADMINISTRATION	Transcutaneous electrical nerve stimulation of the [redacted] nerve at the [redacted] with the Empower Neuromodulation System During the Treatment Phase (Weeks 2-3 of the study), the participant will self-administer a treatment session twice per day. Each treatment session consists of a total of 30 minutes of treatment, with 15 minutes of treatment on one hand followed by 15 minutes on the other hand.
CONTROL PRODUCT, DOSE AND ROUTE OF ADMINISTRATION	No control treatment will be used in this study. However, each participant will serve as his/her own control via data collection during the Baseline Phase (Week 1 of the study). For each participant, treatment effects during the Treatment Phase (Weeks 2 and 3) will be compared with the Baseline Phase.
DURATION OF PARTICIPANT PARTICIPATION AND DURATION OF STUDY	Participants will be on study for up to 35 days **Screening:** up to 7 days **Baseline Phase:** 5-11 days **Treatment Phase:** 11-17 days The total duration of the study is expected to be 9 months. Eight months for participant recruitment and 1 month for final participant follow-up.
STATISTICS **Primary Analysis Plan**	The primary effectiveness endpoint will be change in alcohol consumption as a result of treatment. We will compare averages of daily drinking for the final week of the Treatment Phase (Week 2) vs. the week of the Baseline Phase via a paired t-test.
Rationale for Number of Participants	As a pilot study, the sample size is not based on a formal power calculation. Based on sample sizes for previous pilot studies for neuromodulation studies in addiction and mental health treatment, we aim to recruit 25 participants to obtain a meaningful cohort for a pilot evaluation of the Empower Neuromodulation System.