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High-frequency deep brain stimulation in the treatment of movement disorders

Submission date
06/11/2018

Recruitment status
Stopped

Registration date
11/01/2019

Overall study status
Stopped

Last Edited
03/04/2024

Condition category
Nervous System Diseases

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims:
Deep brain stimulation (DBS) is a well-established treatment for movement disorders and has been used for decades to treat hundreds of thousands of patients around the world. DBS is an accepted treatment in Germany with national guidelines for Parkinson's disease, essential tremor and dystonia movement disorders. A patient with one of these movement disorders may be considered a candidate for DBS surgery when their doctor determines their symptoms of tremor and rigidity are no longer controllable with drug treatment alone. During DBS surgery, small, thin wires (called leads) are inserted into brain areas that are considered responsible for tremor, rigidity and abnormal movements. The most common brain targets for DBS leads are called the globus pallidus internus (GPi), subthalamic nucleus (STN), and ventral intermediate nucleus (Vim). Once the leads are precisely inserted, they are connected to a small stimulator that is implanted under the skin of the chest and turned on to supply a constant supply of electricity to the leads, allowing the therapy to be delivered to the brain. The precise cellular mechanisms of how DBS therapy works are not fully understood, but it is thought that the electricity delivered through the leads to the specific brain targets normalizes electrical communication patterns between neurons in these brain regions that control movement, muscle tone and posture. Commercially available implantable DBS systems allow for stimulation of these brain regions at electrical frequencies between 1-300 Hertz (Hz). These traditional DBS systems are considered 'low frequency' stimulation. Significant symptom improvements for movement disorders using these DBS frequencies is well documented for Parkinson's disease, essential tremor, and dystonia. However, many side effects including paresthesia (tingling throughout the body or in isolated body regions), muscles twitching, balance problems, dysarthria (slurred speech), hemiparesis (weakness in one side of the body), hemiplegia (paralysis in one side of the body), dizziness, lightheadedness, blurred vision, decreased level of consciousness, and seizures have been reported. Furthermore, although the success rate of low frequency DBS is quite high, there are still a significant number of patients who do not benefit from low frequency DBS, or have only temporary benefits with a later symptom recurrence. The Nevro SenzaTM stimulator used in this study works in a similar manner to more conventional DBS stimulators, but can also deliver high frequency 10,000 Hz (HF10) stimulation in addition to traditional lower frequency stimulation. As an established stimulation therapy for chronic pain, HF10 is clinically superior to traditional low frequency both in reducing chronic pain and in limiting common side effects of stimulation, including paresthesia – a tingling sensation that

overlaps the body region(s) being treated – common in low frequency stimulation but not HF10. The aim of this study is to assess the chronic effectiveness and side effects associated with DBS at higher frequencies in reducing movement disorder symptoms including tremor and rigidity.

Who can participate?
Patients aged over 18 with subjects with Parkinson's disease or essential tremor

What does the study involve?
Participants undergo Deep Brain Stimulation (DBS). DBS involves the surgical placement of leads (which look like very thin wires) into the usual DBS targets in subjects with Parkinson's disease or essential tremor i.e. either the ventral intermediate nucleus (VIM), internal globus pallidus (GPi), and subthalamic nucleus (STN). Electrical stimulation is delivered through these wires by a small, battery-operated, rechargeable implanted pulse generator (IPG). Each patient is followed up for 12 months after a successful implantation. The participants attend regular clinic visits to complete questionnaires and assessments and are asked for their feedback on their condition.

What are the possible benefits and risks of participating?
Participants may benefit from the DBS system to improve their condition, i.e. motor symptoms and/or tremor. Deep brain stimulation is an FDA approved and a CE-labeled therapy for the DBS targets indicated in this study. The known risks associated with any DBS system involve the implant procedure, the stimulation parameters, the implanted device, and the remote control. The major risks for any DBS implantation include air embolism, intracranial hemorrhage, and infection. Potential risks related to higher frequency DBS stimulation primarily involves charge safety. Since the pulse width of high frequency stimulation is significantly shorter traditional stimulation, the charge injection is comparable to lower frequency stimulation.

Where is the study run from?
Kliniken der Stadt Köln gGmbH (Germany)

When is the study starting and how long is it expected to run for?
March 2018 to December 2022

Who is funding the study?
Nevro Corp (USA)

Who is the main contact?
1. Dr Sat Pannu (scientific)
2. Mr Wim Laloo (public)

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CA2018EU DBS

Study information

Scientific Title
Prospective, feasibility trial for high-frequency deep brain stimulation in the treatment of movement disorders

Acronym
Senza-DBS

Study objectives
The purpose of this feasibility study is to assess the safety and effectiveness of deep brain stimulation (DBS) using higher frequencies delivered to standard ventral intermediate nucleus (VIM), internal globus pallidus (GPi), and subthalamic nucleus (STN) DBS targets in subjects with Parkinson’s disease or essential tremor.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethik-Kommission Ärztekammer Nordrhein, 22/10/2018, ref: 2018177, Eudamed-Nr: CIV-18-05-024124

Study design
Open-label prospective single-arm feasibility study

Primary study design
Observational

Secondary study design
Case series

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Parkinson’s disease (PD) and essential tremor (ET)

Interventions
This is an open label, prospective, feasibility study to collect data on high-frequency Deep Brain Stimulation (DBS) for the treatment of motor symptoms of Parkinson’s disease (PD) and essential tremor (ET). Stimulation will be delivered using the Senza System. The use of the Senza System for treatment of Parkinson’s disease (PD) and essential tremor (ET) is investigational. Subjects will be consented, enrolled and eligibility criteria checked. If the subject is eligible, the subject will proceed with a Senza system implantation. After successful system implant outcomes will be assessed via standardized assessments at 1 week, 1, 3, 6, 9 and 12 months.

Intervention Type
Device

Pharmaceutical study type(s)
Not Applicable

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
High-frequency Deep Brain Stimulation (DBS)

Primary outcome measure
The feasibility of a future definitive trial is determined using:
1. The number of participants identified, approached, consented and completed, to inform the recruitment and timeline of a future fully-powered study
2. The acceptability and experience of the study process to participants and completion of outcome measures, to refine future study procedures
3. The performance of selected candidate primary outcome measures with respect to level of

acceptability to participants (completion rates, perceived burden) and participant-perceived relevance and value, to determine the optimal primary outcome measure in a future study
4. Data completeness at follow up (participant attrition), standard deviation of the likely primary outcome measure, and the variability of the comparator condition, treatment as usual, across individuals and sites, to estimate sample size for a future study
Measured from enrolment until end of study (12 months follow up).

Secondary outcome measures
Effectiveness and safety are assessed by the following:
1. Motor symptoms are measured using the Unified Parkinson's Disease Rate Scale (UPDRS) at baseline, initial DBS lead implant, device activation, and 1, 2, 3, 6, and 12 month follow-up visits
2. Tremor is measured using the FTM (Fahn-Tolosa-Marin Tremor Rating Scale) at baseline, initial DBS lead implant, device activation, and 1, 2, 3, 6, and 12 month follow-up visits
3. Functioning is measured using the PDQ-39 (Parkinson's Disease Questionnaire-39) at baseline, device activation, and 1, 2, 3, 6, and 12 month follow-up visits
4. Quality of Life in Essential Tremor is measured using the QUEST (Quality of Life in Essential Tremor) questionnaires at baseline, device activation, and 1, 2, 3, 6, and 12 month follow-up visits
5. Neurological status (motor, sensory and reflex functions) is measured using a neurological examination at every visit
6. Incidence of adverse events (AEs) is observed at every visit

Overall study start date
01/03/2018

Completion date
31/12/2022

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
To participate in the study, subjects must meet all of the following inclusion criteria:
1. Have been clinically diagnosed with either bilateral idiopathic Parkinson's disease or unilateral or bilateral essential tremor, which has been refractory to conservative therapy for a minimum of 3 months and completed diagnostic work-up
2. Be 18 years of age or older at the time of enrollment
3. Be an appropriate candidate for the surgical procedures required in this study based on the clinical judgment of the implanting physician
4. Be capable of subjective evaluation; patient must be able to describe and rate his/her disease state progression through the UPDRS
5. Be willing and capable of giving informed consent
6. Be willing and able to comply with study-related requirements and procedures and attend all scheduled visits
7. Have adequate cognitive ability to use a patient programmer and recharger as determined by the Investigator

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
10 study participants with a DBS implant will be evaluated

Total final enrolment
3

Key exclusion criteria
To participate in this study, a subject must not meet any of the following exclusion criteria.
1. Have a medical condition, not intended to be treated with DBS that could interfere with study procedures, accurate UPDRS or FTD reporting, and/or confound evaluation of study endpoints, as determined by the Investigator
2. Have a current diagnosis of a focal brain tumor in a relevant DBS target region or prominent generalized cortical atrophy, as determined by the investigator
3. Have a past medical history significant for seizures, as determined by the investigator
4. Have a current diagnosis or condition such as a coagulation disorder, bleeding diathesis, platelet dysfunction, progressive peripheral vascular disease or uncontrolled diabetes mellitus that presents excess risk for performing the procedure as determined clinically by the investigator
5. Have a condition that would significantly increase perioperative risk including severely diminished functional capacity due to underlying cardiac/pulmonary disease, symptomatic uncontrolled hypertension, symptomatic uncontrolled diabetes mellitus that presents excess risk for performing the procedure as determined clinically by the investigator
6. Any previous history of surgery of ipsilateral basal ganglia surgery (radio frequency or ultrasound lesion or prior DBS implant)
7. Any past medical history suggesting secondary or atypical parkinsonian symptoms including previous cerebrovascular accident, neurotoxin exposure, neuroleptic toxicity, tumor, encephalitis, abnormal iron deposits, or neurologic signs of cerebellar or upper motor neuron involvement or supranuclear gaze palsy
8. Be benefiting from an interventional procedure and/or surgery to treat their movement disorder (Subjects should be enrolled at least 30 days from last benefit)
9. Have an existing drug pump and/or another active implantable device such as a pacemaker
10. Have a condition currently requiring or likely to require the use of diathermy, Transcranial Magnetic Stimulation (TMS) or MRI imaging that is inconsistent with Senza II system guideline in the US manual
11. Have either a metastatic malignant neoplasm or untreated local malignant neoplasm
12. Have a life expectancy of less than one year
13. Have a local infection at the anticipated surgical entry site or an active systemic infection
14. Be pregnant or plan to become pregnant during the study. Women of childbearing potential who are sexually active must use a reliable form of birth control, or be surgically sterile, or be at least 2 years post-menopausal
15. Have a significant untreated addiction to dependency producing medications or have been a substance abuser (including opioids, benzodiazepines, alcohol and illicit drugs) within 6 months

of enrollment
16. Have a metallic aneurysm clip that could interfere with device functioning
17. Have significant cognitive impairment or dementia that would interfere with study compliance or comprehension
18. Have untreated clinically significant depression as evidenced by a self-report score on the Beck Depression Inventory (BDI) II > 20. Patients presenting with depression may also be ruled out by clinical judgement of the investigator
19. Have evidence of acute psychosis or delirium as determined by the investigator
20. Be concomitantly participating in another clinical study

Date of first enrolment
01/02/2019

Date of final enrolment
31/12/2020

Locations

Countries of recruitment
Germany

Study participating centre
Kliniken der Stadt Köln gGmbH
Neufelder Straße 34
Köln
Germany
51067

Sponsor information

Organisation
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Sponsor type
Industry

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http://www.nevro.com

ROR
https://ror.org/02xcxe208

Funder(s)

Funder type
Industry

Funder Name
Nevro Corp

Results and Publications

Publication and dissemination plan
1. Planned presentation of results to international congresses from the start of 2020.
2. Planned publication in a peer-reviewed journal from the end of 2020.

Intention to publish date
31/12/2021

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Sat Pannu.

IPD sharing plan summary
Available on request