Clinical Study of Neuspera*s Implantable Sacral Nerve Stimulation (SNS) System in Patients with Symptoms of Urinary Urgency Incontinence (UUI)

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Primary Efficacy objective: The purpose of the study is to test the efficacy of the Neuspera Implantable SNS System for treatment of urinary urgency incontinence Primary safety objective: The primary safety objective of the study is to assess the...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Bladder and bladder neck disorders (excl calculi)
Study type	Interventional

Summary

ID

NL-OMON54773

Source
ToetsingOnline

Brief title
SANS-UUI Study

Condition

- Bladder and bladder neck disorders (excl calculi)

Synonym
urge to urinate resulting in involuntary urination, urinary urgency incontinence (UUI))

Research involving
Human

Sponsors and support

Primary sponsor: Neuspera Medical Inc.

Source(s) of monetary or material Support: Industrie

Intervention

Keyword: Implant, Neurostimulator, Urinary Urgency Incontinence

Outcome measures

Primary outcome

Efficacy (Phase II):

The primary efficacy endpoint is defined as the percentage of all implanted subjects who experience an improvement in UUI symptoms of at least 50% or more (therapy responders). A therapy responder is defined as experiencing >=50% reduction in the number of UUI episodes at 6 months post-implant, relative to the number of UUI episodes at baseline. Statistical evaluation will be based on a comparison of the percentage of responders to a performance goal of 50%. Calculation of the primary endpoint will be based on the mITT analysis set

Safety (Phase II):

The primary safety endpoint is defined as the incidence of device-related SAEs through the 6-month post-implant visit. The analysis of the endpoint is the proportion of subjects experiencing a device-related SAE through the 6-month post-implant.

Secondary outcome

• Change from baseline in quality of life as measured and assessed by the total ICIQ-OABqol score.

• Change from baseline in mean number of UUI episodes.

• The percentage of subjects who experience an improvement in UUI symptoms

(therapy responders) of at least 50% or more at 12 months visit post implant.

• The percentage of subjects who experience an improvement in ICIQ-OABqol of at least 10 points.

• Change in urgent voids per day. Calculated across all diary episodes with at least mild urgency.

• Change in average number of daily voids from baseline in subjects with at least 8 voids at baseline.

• Change in quality of life measured from baseline as measured and assessed by the ICIQ- OABqol subscale scores.

• Comprehensive summary of all adverse events (AEs) for the duration of study participation.

• Device parameters including but not limited to voltage, pulse width, frequency, and stimulating electrode.

• Physician and subject satisfaction as assessed with the User Experience Questionnaire at 6-month visit post implant.

• Change in Male/Female Lower Urinary Tract Symptoms questionnaire.

• The percentage of subjects with device-related serious adverse events reported through 12-month visit post-implant.

• Change in total urinary output as measured by 72-hour bladder diary.

• Change in fecal incontinence as measured by the Wexner Scale compared to baseline. Calculated in subjects with fecal incontinence.

• Patient Global Impression of Improvement (PGI-I) measured after implant during follow-up.

The following secondary endpoints will be included in a hierarchal analysis of study endpoints and may be intended for labelling claims (all at 6-month visit post-implant follow-up)

• Change from baseline in mean number of UUI episodes

• Change from baseline in ICIQ-OABqol score

• The percentage of subjects who experience an improvement in ICIQ-OABqol of at least 10 points

• Change in urgent episodes per day from baseline. Calculated across all diary episodes with at least mild urgency

• Change in average number of daily voids from in subjects with at least 8 voids at baseline.

• Change in fecal incontinence as measured by the Wexner Scale compared to baseline. Calculated in subjects with fecal incontinence.

Study description

Background summary

Millions of patients worldwide are diagnosed annually with overactive bladder (OAB) including urinary urgency, frequency, nocturia and urgency incontinence (UI). An estimated 546 million patients will be affected by OAB of which 423 million patients will be affected by UI. Many in this patient population are not well controlled by conventional medical management.
Third-line treatments include neuromodulation. Third-line options bridge the treatment gap between conservative therapies for urinary urgency incontinence as a consequence of OAB and irreversible surgical procedures such as enterocystoplasty.
Neuromodulation targets the sacral nerve plexus which regulates control of the bladder and pelvic floor muscles. A neuromodulation treatment currently available for OAB is Sacral Nerve Stimulation (SNS). For SNS therapy, the Medtronic InterStim® Therapy and Axonics systems are indicated for the treatment of urinary retention and the symptoms of OAB. These neurostimulators

are implanted into the lower back, along with the battery powering the stimulator. Device related complications associated with the InterStim® Therapy system include the following: lead migration and fracture, pocket infection, lead infection, pocket pain, cosmetic issues including a budge above the buttocks and requirement for frequent reprogramming. The most frequent adverse events associated with the Axonics system were discomfort due to stimulation, discomfort/heating near the charging area, pain at the neurostimulator site, and lead revision. The most common events reported for the Neuspera system in Phase I of the trial were implant site pain and sensory disturbance.

Study objective

Primary Efficacy objective: The purpose of the study is to test the efficacy of the Neuspera Implantable SNS System for treatment of urinary urgency incontinence
Primary safety objective:
The primary safety objective of the study is to assess the safety of the Neuspera Implantable SNS System for treatment of UUI.

Study design

Prospective, multi-center, single-arm, seamless phased-pivotal study

Intervention

Miniature wireless midfield powered implanted neurostimulation device for urinary urgency incontinence (UUI).

Study burden and risks

Subjects will be required to maintain diaries, and visit the hospital for follow-up visits, where they will complete questionnaires, multiple times during the study.
There are potential risks associated with the Neuspera Implantable SNS System, as listed in section 4.4 of the protocol. Wearing the Wireless Transmitter directly against skin may result in discomfort, irritation, or a burn. The subject may be a non-responder to SNS therapy or the study device may fail to adequately induce therapeutic response. Standard risks associated with minor surgery, including side effects from anaesthesia, post-procedural pain or discomfort, and complications at the incision/injection site such as infection, bleeding, bruising, or swelling, may occur due to the neurostimulator implantation procedure. There may also be risks that are unanticipated at this time.
Testing, safeguards, and safety monitoring have been incorporated into the clinical investigation to further minimize and mitigate the risks.

Neuspera*s SNS System aims to relieve urinary urgency incontinence. If subjects do not respond to the stimulation and don*t obtain relief, they will be exited from the study either after 49 days (for Phase I subjects) so they will only have a short period without effective treatment and a few hospital visit. After this period they can pursue other treatment options that might work for them. For subjects who do respond to the stimulation, they will have obtained relief, and the burden of the follow-up visits is deemed in balance with the benefit they reap from the study.
For Phase II, subjects response rate will be determined at 28 to 42 days. All subjects will continue in the follow-up phase regardless of response rate as an intent to treat analysis will be conducted at 6 months and 12 months of follow-up. A decision to continue a subject with less than a 50% improvement at the end of the 42-day period will be made by the investigator based on what they determine is in the best interest of the subject. Subjects may choose to leave the study at any time to pursue other treatment options that may work better for them.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Is willing and able to understand and has voluntarily signed and dated the current approved informed consent.
2. Is male or female 22 years of age or older.
3. Has a Body Mass Index (BMI) between 18 and 40 kg/m^2.
4. Is a good surgical candidate and is capable of participating in all testing and follow-up clinic visits associated with this clinical study and is capable of independently using the system components as described in the Patient Manual.
5. Is ambulatory and able to use toilet without assistance.
6. Has a diagnosis of UUI for greater than or equal to 6 months prior to the screening baseline visit date.
7. Has a typical residual bladder volume < 150 cc tested within 6 months prior to the screening baseline visit date or is willing to have a test at screening baseline visit.
8. Has urodynamic testing (uroflowmetry, cystometry, and pressure flow) completed within 6 months prior to the screening baseline visit date or is willing to have testing at screening baseline visit.
9. Has cystoscopy test completed within 6 months prior to the screening baseline visit date or is willing to have a test at screening baseline visit.
10. Has failed or was not a candidate for more conservative treatment (e.g,. pelvic floor exercise, biofeedback, behavioral modification).
11. Has failed, could not tolerate (stopped taking medication due to lack of efficacy or intolerable side effects), or not a good candidate for (as determined by treating physician) at least one (1) antimuscarinic or β3 adrenoceptor agonist medication.
12. Is willing and able to washout (at least five half-lives) from OAB medications for a period determined appropriate based on type of OAB medication prior to the baseline bladder diary and remain off OAB medications through the 12-month follow-up visit.
13. Has appropriate sacral anatomy as determined by sponsor*s and investigator*s analysis of radiographic imaging. (The distance from the surface of the skin in the prone and seated position to the bone edge of the S3 foramen must be within the capabilities of the system).
Bladder Diary Inclusion Criteria:
14. Has a diagnosis of UUI with at least 4 UUI episodes on a 72-hour diary, and minimum of 1 UUI episodes per 24-hour period.

Exclusion criteria

1. Has a hemoglobin A1c of >8% or has diabetes mellitus with glucosuria
2. Has diabetic neuropathy.
3. Has interstitial cystitis or bladder pain syndrome as defined by either American Urological Association (AUA) or European Association of Urology (EAU) guidelines, chronic pelvic pain or recurrent symptomatic urinary tract infections.
4. Has skin, orthopedic, neurological or hematological (bleeding disorder) or anatomical limitations that could prevent successful placement of the neurostimulator.
5. Has broken, blistered skin or compromised circulation in the area of the neurostimulator implant.
6. Has neurogenic bladder dysfunction such as traumatic or atraumatic myelopathy, multiple sclerosis, Parkinsonism, or history of cerebrovascular accident.
7. Has documented urinary retention within 6 months prior to the screening baseline visit date.
8. Has clinically significant bladder outlet obstruction.
9. Is currently undergoing or has previously undergone pelvic irradiation.
10. Is a subject with a mechanical obstruction such as benign prostatic hypertrophy, urethral stricture or cancer.
11. Has current grade 3 or 4 pelvic organ prolapse including cystocele, rectocele, , enterocele, procidentia or vaginal vault prolapse.
12. Has symptomatic urinary tract infection (UTI); the subject may be considered for study enrollment if the subject is symptom-free after a full course of treatment prior to beginning the baseline bladder diary. If an asymptomatic bacteriuria is detected during the urinalysis performed at screening, a subject may be enrolled without a waiting period relative to UTI treatment.
13. Has primary stress incontinence or mixed incontinence where the stress component predominates or has been treated surgically for stress urinary incontinence within 6 months prior to the screening baseline visit date.
14. Has received tibial nerve stimulation (TNS) in the past 3 months for the treatment of overactive bladder or unwilling to stay off TNS therapy for 12-month period following implant.
15. Has received treatment of urinary symptoms with any botulinum neurotoxin type-A (BoNT-A) agent in the past 12 months; (e.g. obotulinumtoxinA, Botox,® abobotulinumtoxin A , Dysport,® IncobotulinumtoxinA, Xeomin®)
16. Is a woman who is pregnant or planning to become pregnant during this clinical study or is a woman of child-bearing potential who is not using a medically-acceptable method of birth control. Women of child-bearing potential must undergo a pregnancy test, with clear negative result.
17. Has active substance abuse, including alcohol.
18. Has a known hypersensitivity or contraindication to procedural or post-procedural medications which cannot be adequately managed medically.
19. Has a known hypersensitivity to Neuspera*s SNS System device components.
20. Has previously failed SNS therapy
21. Has active implantable medical devices such as neurostimulators, drug

pumps, pacemakers, or internal defibrillator since compatibility has not been assessed.
22. Has known needs for diathermy (shortwave, microwave, or therapeutic ultrasound), and radiofrequency ablation, in the vicinity of the neurostimulator since these procedures have not been evaluated.
23. Has a known need for therapeutic ultrasound in the area of the sacral nerve neurostimulator as the device can inadvertently concentrate the ultrasound field and cause harm.
24. Has a known need for therapeutic ionizing radiation as the device can damage the electrical components of the sacral nerve stimulator and any damage may not be immediately detectable
25. Has plans to enroll or is currently enrolled in another investigational device or drug trial during his/her participation in this study.
26. The investigator is unable to elicit an appropriate motor response in the subject during the intra-operative testing of the implant procedure.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-03-2020
Enrollment:	12
Type:	Actual

Medical products/devices used

Generic name:	Neuspera□s Implantable Sacral Nerve Stimulation (SNS) System
Registration:	No

Ethics review

Approved WMO Date:	11-11-2019
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	12-02-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	04-03-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	07-07-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-09-2023
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	28-05-2024
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL69260.068.19
Other	The trial has been registered at this time. The trial is registered on www.clinicaltrials.gov: ClinicalTrials.gov Identifier: NCT04232696