A Prospective, Randomized Clinical Trial Evaluating INTIBIA (TM), an Investigational Implantable Tibial Nerve Stimulator, Through 24-Months

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Ethical review	Approved WMO
Status	Completed
Health condition type	Urinary tract signs and symptoms
Study type	Interventional

Summary

ID

NL-OMON56302

Source
ToetsingOnline

Brief title
INTIBIA Pivotal Study

Condition

- Urinary tract signs and symptoms

Synonym
Urgency Urinary Incontinence (UUI); urine loss

Research involving
Human

Sponsors and support

Primary sponsor: Coloplast Corp.

Source(s) of monetary or material Support: Coloplast Corp.

Intervention

Keyword: Implantable tibial nerve stimulator, Neuromodulation / neurostimulation, Randomized, Urgency urinary incontinence

Outcome measures

Primary outcome

The co-primary efficacy endpoints are defined as:

1. The proportion of ITNS-ON subjects achieving >= 50% reduction in urgency urinary incontinence episodes relative to baseline versus a performance threshold (PT) of 50% at 12 months. The endpoint will be considered met if the ITNS-ON treatment group is statistically superior to the PT.

2. The proportion of subjects achieving a >= 50% reduction in urgency urinary incontinence episodes relative to baseline at 3- months. The endpoint will be considered met if the ITNS-ON treatment group is 1statistically superior by a margin of 10% to the ITNS-SHAM treatment group .

Secondary outcome

Secondary Efficacy Endpoints will be tested for superiority of the ITNS-ON group as compared to ITNS-SHAM group in the following order:

• The change in mean urgency score relative to baseline at 3- months.

• The change in mean number of daily voids relative to baseline at 3-months.

Study description

Background summary

Overactive Bladder (OAB) is a condition characterized by symptoms such as urgency urinary incontinence, frequency, urgency, and nocturia. It is not a disease but a collection of symptoms. The prevalence and severity of OAB increase with age, affecting both men and women. Urgency urinary incontinence is reported to be more common in women and is often the most bothersome symptom.

OAB has a negative impact on psychosocial functioning and quality of life. It can affect daily activities, social interactions, and employment. It also impacts sexual function, marital satisfaction, and can lead to increased depression. OAB diagnosis involves ruling out other conditions such as neurological diseases, diabetes, and pelvic organ prolapse through various diagnostic tests.

The treatment of OAB is divided into four categories: behavioral modification, pharmacological treatments, neuromodulation therapies, and invasive interventions. Behavioral therapies include pelvic floor muscle strengthening, journaling, and weight loss. Pharmacological treatments are the second-line option but may have side effects that affect adherence. Neuromodulation therapies, such as sacral nerve stimulation (SNS) and percutaneous tibial nerve stimulation (PTNS), target the innervation system of the lower urinary tract. SNS involves mild electrical impulses delivered to the sacral nerve roots via an implanted neurostimulator, while PTNS stimulates the sacral nerve plexus through the tibial nerve.

Studies have shown that both SNS and PTNS provide improvement in OAB symptoms, with PTNS having fewer side effects and higher success rates compared to SNS. The INTIBIA device is a programmable implantable tibial nerve stimulator (ITNS) that is permanently implanted in the lower calf to deliver electrical pulses to the tibial nerve. A clinical feasibility study of the INTIBIA device demonstrated its safety and efficacy in treating OAB symptoms without any serious adverse events or device deficiencies.

In conclusion, OAB is a collection of symptoms that can significantly impact an individual's quality of life. Treatment options range from behavioral modifications to invasive interventions, with neuromodulation therapies like PTNS showing promising results. The INTIBIA device represents a programmable ITNS with a miniaturized pulse generator and integrated electrode lead that offers a potentially effective and convenient treatment option for OAB patients.

Study objective

The purpose of the INTIBIA pivotal study is to demonstrate the safety and effectiveness of the INTIBIA System in the intended population through 24 months of follow-up. Data at 12-months will be used to support regulatory approval.

The objective of this study is to demonstrate the superiority of ITNS-ON to ITNS-SHAM at 3-months and a performance threshold (PT) at 12-months in the proportion of subjects achieving >=50% reduction in urgency urinary incontinence (UUI) episodes.

Study design

The INTIBIA pivotal trial is a prospective, randomized, sham-controlled, double-blind, multi-center study designed to evaluate the safety and efficacy of an investigational ITNS device in subjects with UUI. Subjects will be randomized to either ITNS-ON or ITNS-SHAM in a 2:1 ratio. Subjects randomized to ITNS-SHAM will cross-over to ITNS-ON after the 3-month study visit and the assessment of the 3-month efficacy endpoints.

Intervention

The intervention is the implantation of the INTIBIA device. The INTIBIA (TM) ITNS is a single-use, programmable implantable tibial nerve stimulator (ITNS) with a miniaturized pulse generator and an integrated electrode lead. The INTIBIA (TM) ITNS is permanently implanted subcutaneously in the medial lower calf, distal to the gastrocnemius muscle. The electrode lead provides electrical pulses to the tibial nerve at a point 5 to 6 centimeters proximal to the medial malleolus. The pulse generator autonomously provides neuromodulation at a pre-set pulse pattern and frequency preset to match those of Percutaneous Tibial Nerve Stimulation (PTNS), without requiring patient or physician intervention post-operatively. The purpose of this intervention is to assess the effectiveness of the ITNS device in managing symptoms of Overactive Bladder (OAB) and improving the quality of life for the study subjects.

Study burden and risks

Burden:

Participation in the study may involve undergoing a surgical procedure for the implantation of the INTIBIA ITNS device.
Subjects will need to adhere to pre-operative and post-operative instructions, which may include discontinuation of blood thinners, antiseptic scrubbing, wearing a compression sock, and avoiding certain activities for a period of time.
The study requires subject follow-up comprising multiple visits over a minimum of 24-month period, which may require time and effort from participants.

Screening tests such as catheterization and cystoscopy may be performed, which can cause temporary discomfort or potential risks.
Participants may need to share personal information during the study, which should be kept private and confidential.

Risks:

The implantation procedure carries risks typical of percutaneous implantation procedures, such as infection, nerve/tissue/vessel damage, migration or malfunction of the implanted device, and pain at the implant site.
There is a potential risk of the device being ineffective, resulting in the continuation of UUI symptoms despite the intervention.
Screening tests like catheterization and cystoscopy carry their own risks, including urinary tract infection, discomfort, urethral injury, and other potential adverse effects.

Benefits:

The potential benefits of participation include the improvement of OAB symptoms, such as urgency urinary incontinence episodes, urinary urgency symptoms, frequency of voids per day, and nocturia episodes.
Participation contributes to the advancement of scientific and clinical knowledge regarding the safety and effectiveness of the INTIBIA ITNS device.
Positive study results can potentially lead to improvements in the technical capabilities and clinical practices for third-line OAB therapy.
There is the potential for future patients to benefit from the availability of the INTIBIA ITNS device for routine use.

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. Women or men 22-80 years of age
2. Symptoms of overactive bladder with urgency urinary incontinence (UUI) demonstrated on a 72-hour voiding diary defined as a minimum of four (4) leaking episodes associated with urgency, and at least one leaking episode each 24-hour period
3. Greater than or equal to 6-month history of UUI diagnosis
4. Failure of conservative or behavioral therapy (e.g., bladder diet, timed voiding, bladder training, bladder control strategies, pelvic floor muscle training, fluid management)
5. Willing to abstain from OAB medications for the duration of the study
6. Willing to maintain a stable dose of all other medications that affect bladder function (e.g., tricyclic antidepressants) for at least four (4) weeks prior to beginning the baseline voiding diary and baseline questionnaires
7. Ambulatory and able to use the toilet independently and without difficulty
8. Willing and capable of providing informed consent
9. Willing and able to complete all procedures and follow-up visits indicated in the protocol

Exclusion criteria

1. Diagnosis of stress urinary incontinence or mixed urinary incontinence, as confirmed by cough stress test and with a response of Yes to Q3 on the UDI-6 questionnaire
2. Current symptomatic urinary tract infection (UTI), urethritis, or more than three (3) UTIs in past year
3. Have post-void residual urine volume >30% of total voided volume
4. Inadequate skin integrity or any evidence of an infection, edema or

inflammation in either lower leg
5. Evidence of anatomic abnormalities that could jeopardize the placement of the device or pose a hazard to the subject
6. Prior treatment of urinary symptoms with nerve stimulation (e.g., percutaneous tibial nerve stimulation [PTNS] or sacral nerve stimulation [SNS])
7. History of chronic pain (e.g., chronic pelvic pain, fibromyalgia, Lyme disease, chronic back pain)
8. An active implantable electronic device regardless of whether stimulation is ON or OFF
9. Treatment of urinary symptoms with botulinum toxin therapy within twelve (12) months
10. Anyneurologicalconditionthatcouldinterferewithnormalbladderortibialnervefunction,including stroke, epilepsy, multiple sclerosis, Parkinson*s disease, peripheral neuropathy, fibromyalgia, or spinal cord injury (e.g., paraplegia)
11. Current urinary tract mechanical obstruction (e.g.,benign prostatic enlargement or urethral stricture)
12. Other urinary tract dysfunction (e.g.,abnormal upper urinary tract function, vesicoureteral reflux, bladder stone or tumor, urinary fistula)
13. Endstage renal failure,GFR<35, or dialysis
14. History of pelvic cancer within the past two years
15. Pelvic organ prolapse at or beyond the hymenal ring
16. InterstitialcystitisorbladderpainsyndromeasdefinedbyeitherAmericanUrologicalAssociation (AUA) or European Association of Urology (EAU) guidelines prior to INTIBIA implant date
17. Diabetes with peripheral nerve compromise or uncontrolled diabetes
18. Pregnant as confirmed by urine or serum pregnancy test, plans to become pregnant over the study period, is less than one-year post-partum, is breast-feeding
19. Current active or a chronic systemic infection
20. Condition requiring magnetic resonance imaging(MRI) of lower leg
21. Condition requiring diathermy
22. Allergy to polyethylene terephthalate, silicone rubber, platinum, iridium, or polyurethane
23. Allergy to local anesthetic or adhesives
24. Deemedunsuitableforenrollmentbytheinvestigatorbasedonhistoryorphysicalexamination(e.g., bleeding disorders, current anticoagulant medications)
25. Enrolled in another investigational or interventional device or drug trial over the study period

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	19-01-2024
Enrollment:	36
Type:	Actual

Medical products/devices used

Generic name:	The INTIBIA (TM) ITNS
Registration:	No

Ethics review

Approved WMO

Date:	21-11-2023
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
ClinicalTrials.gov	NCT05250908
CCMO	NL84762.100.23