Prospective, non-randomized, multicentre clinical evaluation of the recharge free Axonics SNM System (INS Model 4101)

Published: 13-02-2025
Last updated: 22-02-2025

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Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON57301

Source
ToetsingOnline

Brief title
F15 Prospective Study

Condition

- Other condition
- Bladder and bladder neck disorders (excl calculi)
- Renal and urinary tract therapeutic procedures

Synonym
Loss of bladder control; bowel leakage

Health condition

Bladder and Bowel Dysfunctions

Research involving
Human

Sponsors and support

Primary sponsor: Axonics, Inc.
Source(s) of monetary or material Support: industry;Axonics;Inc.

Intervention

Keyword: Fecal Incontinence (FI), Urinary Frequency, Urinary Urge Incontinence (UUI)

Outcome measures

Primary outcome

SAFETY ENDPOINTS

Early and late incidence rates will be reported for the following:

• All Serious Adverse Events (SAEs)

• Device-related Adverse Events

• Procedure-related Adverse Events

An Independent Physician Adjudicator (IPA) will evaluate adverse events that are endpoint related as well as those resulting in death, device deficiencies, explants or revisions. The IPA will adjudicate events for their relatedness to the investigational device and/or the surgical procedure.

PERFORMANCE/EFFECTIVENESS ENDPOINTS

Primary Effectiveness

• For OAB: International Consultation on Incontinence Questionnaire Overactive Bladder quality of life Module (ICIQ-OABqol)

Demonstrate an improvement in Questionnaire Health-Related Quality of Life (HRQL) total score at 3 months post-implant compared to baseline

• For FI: Fecal Incontinence Quality of Life (FIQOL) and Cleveland Clinic Florida Fecal Incontinence Score (CCF-FIS)

Demonstrate an improvement in FIQOL and CCF-FIS (if participant had a score of >=6 at baseline) at 3 months post-implant compared to baseline

Secondary outcome

Secondary Effectiveness

• For OAB: ICIQ-OABqol

Demonstrate an improvement in HRQL total score at 1-year post-implant compared to baseline

• For FI: FIQOL and CCF-FIS

Demonstrate an improvement in FIQOL and CCF-FIS (if participant had a score of

>=6 at baseline) at 1-year post-implant compared to baseline

Study description

Background summary

INTRODUCTION AND BACKGROUND

Sacral Neuromodulation (SNM) is a guideline-recommended treatment for Overactive Bladder (OAB) including urinary urgency incontinence (UUI) and urinary frequency (UF), and for nonobstructive urinary retention (NOUR) and fecal incontinence (FI). While these conditions are not life-threatening, they do have a significant impact on quality of life and may limit a person from being able to participate in daily activities. Long-term data support the safety, efficacy, and durability of the therapy. Recent innovations in SNM therapy, such as a long-lived device and the ability to undergo a full body MRI, have made the therapy more accessible and attractive to patients and physicians. This section describes the clinical background of overactive bladder and fecal incontinence as well as guideline-recommended treatment options.

Overactive Bladder (OAB)

Overactive bladder is a chronic condition that encompasses several bothersome urinary symptoms that may occur alone or in combination. The hallmark symptom of OAB is urinary urgency, a sudden compelling urge to urinate that is difficult to defer. Urgency may lead to one or more OAB symptoms, including:

-Urinary frequency (voiding 8 or more times a day)

-Urinary urgency incontinence (involuntary loss of urine associated with a sudden compelling desire to void)

According to the European Institute of Women*s Health, approximately 60 million adults experience urinary incontinence which is twice as common on women than in men. The European Association of Urology Guidelines (EAU) refers to conditions such as overactive bladder, stress urinary incontinence and mixed urinary incontinence as Lower Urinary Tract Symptoms (LUTS). In the US, OAB has been estimated to affect over 40 million adults and the prevalence increases with age in both men and women. It has been estimated that less than 50% of patients suffering from OAB seek treatment and that up to 80% discontinue OAB medications within one year of initiation. Although not life-threatening, OAB can have a significant impact on a patient*s quality of life, as well as having medical consequences associated with this condition including a higher risk of

falls and hip fractures which increase by 28% and 32% respectively.

The Guidelines state that most cases of OAB can be diagnosed based on history, physical exam, and a urinalysis. Initiation of non-invasive treatment does not require an extensive evaluation. In some patients, additional evaluation and diagnostic procedures may be necessary to validate an OAB diagnosis, exclude other disorders and fully inform the treatment plan. These may include a urine culture, post-void residual, bladder diaries, cystoscopy, and/or urodynamics. The most common cause of OAB is considered to be idiopathic. For these patients, the EAU guidelines provide a strong rating and recommend SNM for patients who have OAB refractory to medications. The AUA guidelines list SNM as a third-line therapy for patients who have failed conservative therapy and medications.

Fecal Incontinence (FI)

According to the American Society of Colon and Rectal Surgeons, fecal incontinence is generally defined as the uncontrolled passage of feces for a duration of at least 3 months in an individual who previously had control3. Other common terms used to describe this condition include anal incontinence and accidental bowel leakage. The prevalence of FI varies widely depending on the specific definition used and the population surveyed, ranging between 1.4% and 18% in women. FI in men is not as prevalent and is most commonly a result of evacuatory dysfunction and rectal hyposensitivity.

The highest incidence of incontinence is reported in nursing home populations, in which rates of FI can reach as high as 50%. A notable fact is that FI is the second leading cause of nursing home placement in the United States. Fecal incontinence is a very undertreated condition that can have a severe impact on quality of life, yet less than one-third actually seek medical care. Of those that do, more than half do so with their primary care provider who often is unaware of advanced treatment options such as SNM. Causes of FI are multifactorial and include four main categories: anatomical (e.g., anal sphincter trauma, rectal mucosal prolapse), neurological (pudendal nerve injury, diabetes), functional (chronic diarrhea), and idiopathic. Most causes are likely multifactorial and fall under the idiopathic category. Treatment options are limited and are dependent on the underlying etiology. Both the American Society of Colon and Rectal Surgeons as well as the American College of Gastroenterology have a strong recommendation for SNM for patients who have failed conservative therapy.

Study objective

The objective of this trial is to confirm that there are no new safety and performance outcomes for participants receiving the Axonics SNM System INS Model 4101 for the treatment of OAB and FI. The only notable difference between the existing, approved INS Model 1101, also known as R15, and Model 4101, known

as F15, is that Model 4101 is a non-rechargeable system (due to using a primary cell battery) whereas Model 1101 uses a rechargeable battery source that requires monthly recharging by the patient. The mechanism of action is identical in that the therapy is delivered to the sacral nerve, typically the 3rd sacral nerve root,. Both models use the same exact stimulation waveform.

Study design

This clinical pivotal trial is a single-arm, multi-center, prospective, non-randomized trial to be conducted throughout Europe and the United States. Regulatory approval will be obtained in each region prior to the start of the trial in that region. If specific requirements are identified beyond those already defined in the body of this protocol, they may be added to the protocol in an Appendix and will be applicable to that region only.

Participants with primary diagnosis of OAB and FI who require an Axonics SNM device will be included. Participants must meet the eligibility requirements specified in this protocol. Up to 110 participants (approximately 55 for each indication) will be enrolled and implanted at 20 participating sites. Per physician discretion, participants may undergo an external trial period prior to full implant. The data collected for the study endpoints will be submitted for each indication separately once completed for that indication.

Safety and performance/effectiveness data will be analyzed when participants have completed the protocol-specified timepoint (e.g., upon 3-month primary endpoint completion for each indication) and will be submitted to the Notified Body/Approved Body for review and product approval in Europe. Participants will continue follow-up in the trial per the visits specified in this protocol. Once all participants have completed the 12-month secondary endpoint, the complete trial data set will be submitted to the applicable IRB/EC and regulatory agencies and the participants will exit the trial. Active participants may then consent to be enrolled in a post-market clinical follow-up study sponsored by Axonics, Inc. as approved by the applicable IRB/EC and regulatory agencies.

Intervention

The Axonics SNM System is an implantable device comprised of implantable and non-implantable components. The implantable Neurostimulator (INS) (Model 4101) is a non-rechargeable device which provides electrical pulses to stimulate the sacral nerve. It is connected to the Axonics Tined Lead, which conducts stimulation pulses from the INS to a sacral nerve, typically the 3rd and occasionally the 4th sacral nerve root.

The indicated duration of the device is 15 years; however, this can vary depending on the energy use settings.

The Axonics SNM system includes the following non-implantable components:

1801 Lead implantation kit

2301 Patient Remote Control

2501 Clinician Programmer

Study burden and risks

The benefits of the INS Model 4101 include reducing symptoms of bladder and bowel dysfunctions and improvement in quality of life. One additional benefit of Model 4101 is that it has a primary cell battery in which the patient does not need to charge their device.

As with all SNM devices, serious complications may occur including risks that could require a reoperation (revision) and/or explant of the device.
This clinical investigation will be conducted under the direction of qualified physicians experienced with SNM surgery including the Axonics SNM System. All participating investigators and sites are screened and qualified. They must be experienced in conducting clinical research and have adequate personnel to ensure compliance to this protocol. No special training is required to implant the INS Model 4101 given the investigators selected are experienced using both Axonics and other SNM devices.

Additional burden to study participants will be as follows:
- Attending study required follow-up visits
- Traveling to the study sites for study required follow-up vists
- Completing Quality-of-Life Questionnaires
- Completing Participants Satisfaction Questionnaire

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. 18 years or older
2. Provides written informed consent prior to trial procedures
3. Primary indication of OAB (UUI/UF) or FI
4. Willing and capable to provide informed consent
5. Agrees to attend all follow-up assessments for up to 1 year and is willing to comply with specified evaluations at clinical investigational sites that are participating in this trial

Exclusion criteria

1. Any significant medical condition that is likely to interfere with trial procedures, device operation, or likely to confound evaluation of trial endpoints (includes neurological conditions such as multiple sclerosis)
2. Any psychiatric or personality disorder that is likely to interfere with trial procedures at the discretion of the participating physician; this may include poor understanding or compliance with trial requirements
3. History of allergic response to titanium, zirconia, polyurethane, epoxy, or silicone
4. A female who is breastfeeding
5. A female with a positive urine pregnancy test

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	25-11-2024
Enrollment:	8
Type:	Anticipated

Medical products/devices used

Generic name:	Axonics SNM System (IPG Model 4101)
Registration:	No

Ethics review

Approved WMO

Date:	13-02-2025
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NCT06186765
CCMO	NL86298.000.24