A post-market clinical follow up of the Genio® System for the treatment of Obstructive Sleep Apnea in adults

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The primary objective of this study is to confirm the safety and clinical effectiveness of the Genio® system in moderate to severe Obstructive Sleep Apnea (OSA) adult patients over a period of 5 years post-surgery.

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

Summary

ID

NL-OMON55961

Source
ToetsingOnline

Brief title
EliSA

Condition

- Other condition

Synonym
sleep-related breathing disorder, Transient cessation of respiration during sleep

Health condition

Obstructive Sleep Apnea disorders

Research involving
Human

Sponsors and support

Primary sponsor: Nyxoah NV
Source(s) of monetary or material Support: Nyxoah

Intervention

Keyword: Hypoglossal nerve stimulation, Obstructive Sleep Apnea

Outcome measures

Primary outcome

Primary Safety Endpoint:

Safety will be assessed to track the long-term safety of the Genio® System

according to the Genio® System Post Marketing Surveillance Plan.

Safety will be evaluated by the incidence of device-related SAEs recorded

during the study for a period of 12 months post-surgery. No formal statistical

hypothesis will be tested as part of the safety assessment.

Safety evaluation will be done both at local (by Investigator) and central

level (supported by an independent Clinical Events Committee (CEC)).

Co-Primary Effectiveness Endpoints:

Effectiveness will be assessed to track the performance of the Genio® System

according to the Genio® System Post Marketing Surveillance Plan.

• Change in AHI from baseline to 12 months post-surgery

• Change in the quality of life measured by the Functional Outcomes of Sleep

Questionnaire (FOSQ-10) from baseline to 12 months post-surgery

Secondary outcome

• Change in ODI from baseline to 12 months post-surgery

• Change in the percentage of sleep time at SaO2 < 90% from baseline to 12 months post-surgery

• Change in the quality of life measured by the Symptoms of Nocturnal Obstruction and Related Events (SNORE-25) questionnaire from baseline to 12 months post-surgery

• Change in daytime sleepiness measured by the ESS questionnaire from baseline to 12 months post-surgery

• Change in AHI from baseline to 2-, 3-, 4- and 5-years post-surgery

• Change in ODI from baseline to 2-, 3-, 4- and 5-years post-surgery

• Change in the percentage of sleep time at SaO2 < 90% from baseline to 2-, 3-, 4- and 5-years post-surgery

• Change in OSA-specific quality of life measured by the FOSQ-10 questionnaire from baseline to 2-, 3-, 4- and 5-years post-surgery

• Change in OSA-specific quality of life measured by SNORE-25 questionnaire from baseline to 2-, 3-, 4- and 5-years post-surgery

• Change in daytime sleepiness measured by the ESS questionnaire from baseline to 2-, 3-, 4- and 5-years post-surgery

• Compliance in device usage over time through completion of a patient diary

Study description

Background summary

OSA is a respiratory sleep disorder characterized by recurrent episodes of partial (hypopnea) or complete (apnea) obstructions of the upper airway.

These obstructions caused by the relaxation and gradual collapse of the pharyngeal muscles, result in reductions or cessations of the respiratory airflow and therefore, in blood oxygen desaturations.
The largest upper airway dilator muscle is the genioglossus muscle, one of the different tongue muscles, and is responsible for forward tongue movement and stiffening of the anterior pharyngeal wall. In people with OSA, the neuromuscular activity of the genioglossus muscle is decreased compared to normal individuals, accounting for insufficient response and contraction to open the airway. This important factor contributes to airway obstruction; the pharyngeal muscles relax, gradually obstruct the airway, and can completely block or significantly restrict air flow.
OSA is the most common sleep disorder and is associated with major comorbidities. The gold standard diagnosis method for OSA is the overnight PSG that monitors many body functions during sleep such as brain activity (Electroencephalogram [EEG]), heart rhythm (Electrocardiogram [ECG]), muscle activation (Electromyogram [EMG]), eye movement (Electrooculogram [EOG]), oxygen level (oximetry), snoring intensity, and respiratory flow and effort.
In OSA patients, airway obstruction events occur several times during the night. These obstruction events consist of apneas and hypopneas and lead to a gradual decrease of oxygen levels in the blood, which in turn results in a decrease of heart rate. Arousals occur in the setting of hypoxemia.
These arousals are registered by the EEG and show that the brain awakes from any stage of sleep to a short arousal. At this time, there is a conscious breath or gasp, which resolves the episode. An increase in sympathetic tone activity mediated through the release of hormones such as epinephrine and noradrenaline occurs. As a result of the increase in sympathetic tone, the heart enlarges in attempt to pump more blood and increase the blood pressure and heart rate.
These repeated arousals combined with repeated hypoxemia leaves the patient sleep deprived, which leads to daytime somnolence and worsens cognitive function. This cycle can repeat itself hundreds of times per night in patients with severe OSA. These repeated fluctuations in sympathetic tone and nocturnal episodes of elevated blood pressure night may evolve into sustained hypertension. Elevated high blood pressure and increased heart rate can in turn result in other diseases. The Oxygen Desaturation Index (ODI) is a commonly used metric used to assess the severity of OSA and is defined, according to the 2014 recommended guidelines from the American Academy of Sleep Medicine (AASM), as the number of times per hour of sleep that the blood's oxygen level drop by at least 3% from baseline.
Apnea-Hypopnea index (AHI) is a standard common measure used to assess the severity of OSA that corresponds to the average number of episodes of apnea and hypopnea per hour of sleep. An apnea event is defined as a breathing cessation (>=90% airflow decrease) lasting 10 seconds or more. A hypopnea event is defined as an airflow decrease >=30% for > 10 seconds and >=3% desaturation or arousal. AHI severity is classified as 5-15, 15-30, and >30 events/hour indicating mild, moderate and severe levels of OSA respectively.

Study objective

The primary objective of this study is to confirm the safety and clinical effectiveness of the Genio® system in moderate to severe Obstructive Sleep Apnea (OSA) adult patients over a period of 5 years post-surgery.

Study design

This study is a multicenter, prospective, single arm, non-randomized, post-market study.
Duration of the study is expected to take up to 8.5 years. Recruitment phase is expected to take between 30 and 42 months and each patient will be followed for safety and effectiveness for 5 years post-surgery. The primary outcomes will be assessed at 12 months, but treatment effects, and safety will be evaluated for an additional 4 year period.
A patient is considered to have completed the study if they have completed the last visit, 5 years post-surgery.
The study will be completed once the last patient in (LPI) will have successfully reached the 5 years follow up period.

Intervention

All eligible patients will be implanted with the Genio system and therapy will be individually optimized.

Study burden and risks

It is expected that patients will experience an improvement in their sleep apnea after device activation.
Patients participating in the study will be required to come at the hospital for screening activities. If they are eligible, they will then come for the surgery, the device activation and follow up visits including setup for home PSGs (at 5 visits). At 7 visits in total, they should complete OSA questionnaires (FOSQ-10, ESS, and SNORE-25). They will also complete the Patient Usability and Patient Satisfaction questionnaires 8 and 5 times respectively. In addition, patient diary should be completed daily from the activation of the device up to 12 months post-surgery. They will also receive 4 phone calls of about 15 minutes to assess their general wellbeing including collection of any emerging AEs.

Contacts

Public
Nyxoah NV

Rue Edouard Belin 12
Mont-Saint-Guibert 1435
BE
Scientific
Nyxoah NV

Rue Edouard Belin 12
Mont-Saint-Guibert 1435
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

A patient must meet all of the following inclusion criteria to be eligible for inclusion in this study:
1. Age above 18 years.
2. Body Mass Index (BMI) < 35 kg/m2.
3. Cricomental space positive (>= 0 cm). The cricomental space is the distance between the neck and the bisection of a line from the chin to the cricoid membrane when the head is in a neutral position.
4. AHI between 15 to 65 events/hour documented by the closest PSG performed at the time of patient ICF signature and within maximum 12 months of screening (as long as the patient stays within ±4kg of their initial weight and has no additional significant comorbidities) and fulfilling the required technical criteria or during the screening phase.
5. Non-Positional OSA as per investigator*s assessment or the patient has either not tolerated, has failed or refused positional therapy.
6. Combined central and mixed AHI < 25% of the total AHI.
7. Has either not tolerated, has failed or refused Positive Airway Pressure (PAP) or Mandibular Advancement Device (MAD) treatments.
8. Written informed consent obtained from the patient prior to performing any study specific procedure.

9. Willing and capable to comply with all study requirements, including specific lifestyle considerations, performing all follow-up visits and sleep studies, evaluation procedures and questionnaires for the whole duration of the trial.

Exclusion criteria

Patients meeting any of the following criteria will be excluded from participation in this study:
1. Inadequately treated sleep disorders other than OSA that would confound functional sleep assessment:
a. Severe chronic insomnia,
b. Insufficient sleep syndrome,
c. Narcolepsy,
d. Restless legs syndrome,
e. REM behavior disorder,
f. Others deemed sufficient disorders that would confound functional sleep assessment in the judgment of the Investigator.
2. Taking medications that in the opinion of the Investigator may alter consciousness, the pattern of respiration, or sleep architecture.
3. Major anatomical or functional abnormalities that would impair the ability of the Genio® system to treat OSA:
a. Craniofacial abnormalities narrowing the airway or the implantation site,
b. Palatine tonsil size 3+ or 4+ by the Brodsky Classification,
c. Relevant fixed upper airway obstructions (tumor, polyps, nasal obstruction),
d. Complete concentric collapse of the soft palate observed during Drug-Induced Sleep Endoscopy (DISE) performed within maximum 24 months of screening and fulfilling the required technical criteria or during the screening phase.
e. Congenital malformations in the airway,
f. Hypoglossal nerve palsy (bilateral limited tongue movement, or unilateral unintended tongue deviation during protrusion),
g. Others deemed sufficient to impair the ability of the Genio® system to treat OSA in the judgment of the Investigator.
4. Inadequately treated psychiatric disease (e.g., psychotic illness, uncontrolled major depression or acute anxiety attacks) that prevents patient compliance with the requirements of the investigational study testing.
5. Severe history of drug or alcohol abuse within the previous 3 years.
6. Life expectancy < 12 months.
7. Any medical illness or condition that contraindicates a surgical procedure under general anesthesia in the judgment of the investigator, or that would prevent the implantation of the Implantable Stimulator or the placement of Activation Chip/Disposable Patch.
8. Prior surgery or treatments that could compromise the effectiveness of the Genio® system:
a. Airway cancer surgery or radiation,

b. Mandible or maxilla surgery in the previous 3 years (not counting dental treatments),
c. Other upper airway surgery to remove obstructions related to OSA in the previous 3 months (e.g., uvulopalatopharyngoplasty (UPPP), tonsillectomy, nasal airway surgery),
d. Prior hypoglossal nerve stimulation device implantation.
9. Has an Active Implantable Medical Device (AIMD) even if the device can be temporarily turned off.
10. Participation in another clinical study (excluding registries) during the study period (5 years) with an active treatment arm that could confound the results of the EliSA study.
11. Plan to become pregnant, currently pregnant, or breastfeeding during the study period (5 years).
12. Vulnerable populations will not be considered for inclusion in this study.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	09-07-2020
Enrollment:	25
Type:	Actual

Medical products/devices used

Generic name:	The Genio® system
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	23-04-2020
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-01-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-02-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-07-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-09-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-10-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-01-2024
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-05-2024
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-02-2025
Application type:	Amendment
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	NCT04031040
CCMO	NL70641.100.19