Early results from a multicenter, prospective study using dual-sided hypoglossal nerve stimulation for the treatment of obstructive sleep apnea

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CAUTION – Investigational device. Limited by United States law to investigational use.

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INTRODUCTION

Hypoglossal nerve stimulation (HGNS) is an alternative option for patients intolerant to positive airway pressure (PAP), the first-line treatment for obstructive sleep apnea (OSA). A multicenter study ("DREAM") to assess the safety and efficacy of a bilateral hypoglossal nerve stimulation system is reported.

METHODS

- Participants with moderate-to-severe OSA were implanted with a bilateral HGNS system in a multicenter, prospective, open-label study. Participants had either failed or refused PAP therapy and did not exhibit complete concentric collapse of the soft palate during drug-induced sleep endoscopy (DISE).
- Co-primary endpoints of the study include ≥50% reduction in apnea–hypopnea index (AHI) and a residual AHI<20 ("Sher criteria") and ≥25% reduction in oxygen desaturation index (ODI) compared to baseline OSA severity as measured with fixed therapeutic settings during a full-night polysomnography (PSG) based on 2012 AASM scoring guidelines. DISE and PSG studies were scored by independent core laboratories.
- Protocol was approved by institutional review boards or central/medical ethics committees. All participants provided written informed consent at enrollment. Safety data was reviewed and adjudicated by independent entities: a clinical events committee and a data and safety monitoring board. An independent statistician generated the data presented in this abstract.

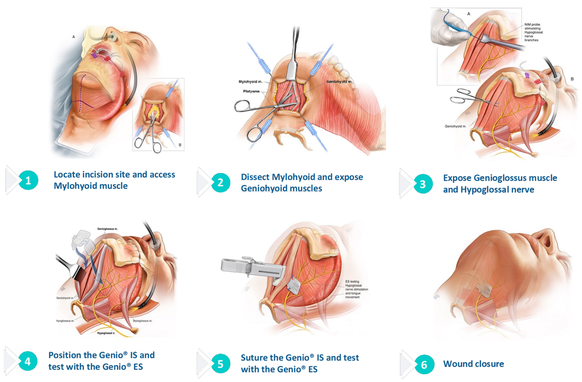

Figure 1. Step-by-step implant procedure for the Genio Neurostimulation system (Nyxoah SA, Belgium) for the treatment of obstructive sleep apnea. The implantable stimulator (IS) has two sets of electrodes which are positioned over the medial branches to stimulate the hypoglossal nerve. The images are for illustrational purposes only and it should be appreciated that surgical anatomy might differ between patients thereby requiring adjusted placement over the respective area of the hypoglossal nerve.

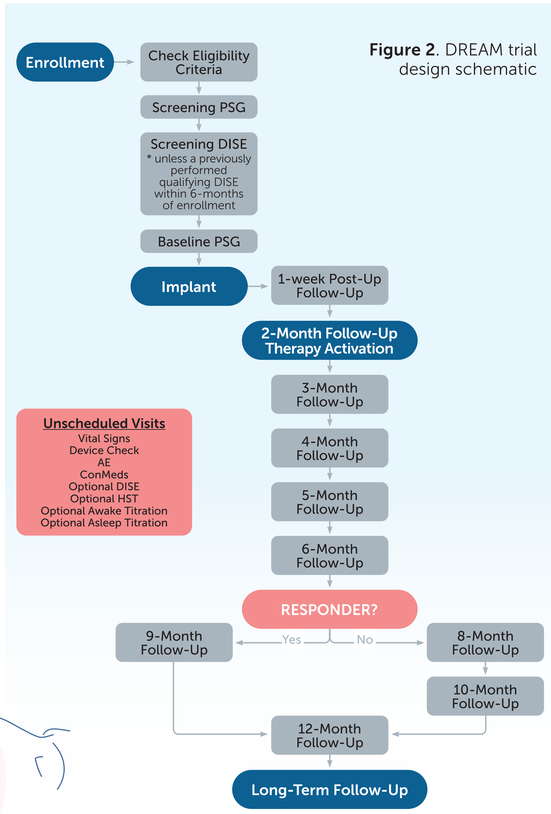

Figure 2. DREAM trial design schematic

Major Inclusion Criteria	**1**. Age from 22 to 75 years (inclusive). Participant cannot be under guardianship, under curatorship or under judicial protection. **2**. Body mass index (BMI) ≤ 32 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**. Has either not tolerated, has failed or refused positive airway pressure (PAP) treatments. **5**. Moderate to severe OSA (15≤AHI4≤ 65 where combined central and mixed AHI < 25% of the total AHI) based on a screening PSG. **6**. Non-supine AHI > 10 events on the screening PSG or participant has either not tolerated, has failed or refused positional therapy.
Major Exclusion Criteria	**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. **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/the implantation site, b) Palatine tonsil size 3+ or 4+ by the Brodsky Classification, c) Fixed upper airway obstructions, d) Congenital malformations in the airway, e) Hypoglossal nerve palsy, f) Existing swallowing difficulty as measured by a score of ≥3 on the EAT-10 questionnaire **4**. Significant comorbidities that contraindicate surgery or general anesthesia: a) Revised Cardiac Risk Index Class III or IV, b) Persistent uncontrolled hypertension despite medications, c) Coagulopathy or required anticoagulant medications that cannot be safely stopped in the perioperative period, d) Degenerative neurological disorder, e) Diagnosed psychiatric disease that prevents participant compliance with the requirements of the investigational study testing, f) Substance or alcohol abuse history within the previous 3 years, g) Any other chronic medical illness or condition that contraindicates a surgical procedure or general anesthesia in the judgment of the investigator. **5**. 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 5 years, 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. **6**. Has an Active Implantable Medical Device even if the device can be temporarily turned off. **7**. Plan to become pregnant, currently pregnant, or breastfeeding during the study period.

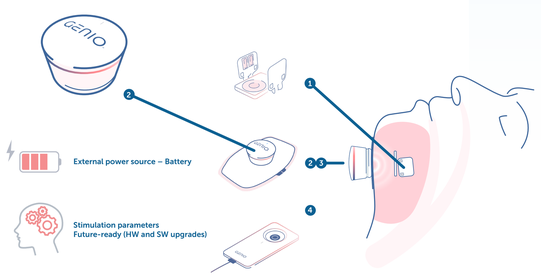

Figure 3. Figure 3. Schematic of Genio system. (**1**) Implantable stimulator (IS); (**2**) Activation chip (AC); (**3**) Disposable patch (DP); (**4**) Charging unit (CU)

RESULTS

A total of 115 of 685 (16.8%) consented participants were implanted with the bilateral HGNS system across 20 clinical sites. Mean age, AHI and body mass index for the participants were 56.7±7.4 years, 28.1±12.4/hr and 28.6±2.6 kg/m², respectively.

Thirty-four (29.6%) evaluable subjects have either completed their M12 PSG or exited the study as of the drafting of this abstract. A partial CONSORT flow diagram of the study subject progress through various timepoints.

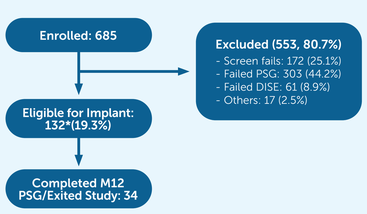

Figure 4. CONSORT flow diagram of study subject progress. Enrollment-to-implant ratio was 17.4%. Rates of failed PSGs and failed DISEs for CCC were 44.2% and 8.9%, respectively.

* Seventeen subjects were withdrawn, lost to follow-up either post-DISE or post-baseline PSG, not attempted an implant either due to site closure(s) or completion of target implant numbers.

SAFETY DATA

- Reported for all 685 enrolled participants
- Unanticipated adverse device effects (UADEs): None
- Serious adverse events (SAEs): 13 (device-related:2)
- Non-serious adverse events: 252
- Explants prior to 12-month visit: 3 (migration/possible migration:2, no response to stimulation:1)

Relatedness of SAE	Number of Events
Device-related	2*
Procedure-related	6 (Definitely: 5, Probably: 1)*
Unrelated to both device- & procedure-related	6
TOTAL	13

* Includes an SAE that is both device- and procedure-related.

EFFICACY DATA

Twenty-two (64.7%) and twenty-six (76.5%) subjects who had either completed a full-night PSG or exited study 12-months post-implant were AHI and ODI responders, respectively.

CONCLUSIONS

Early incomplete results from a pivotal clinical study assessing safety and efficacy of bilateral HGNS in OSA are reported.

SUPPORT *(if any)*

The study was sponsored by Nyxoah, Inc.

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