INFORMATION FORM FOR PARTICIPANT

Study title: "Assessment of the effect of hypoglossal nerve stimulation therapy on the site of collapse during drug-induced sleep endoscopy"

Study sponsor: Antwerp University Hospital, Department of Otorhinolaryngology and Head & Neck Surgery, Drie Eikenstraat 655, 2650 EDEGEM

Committee for Medical Ethics: Ethical Committee UZA

Primary research physician: Prof. Dr. Vanderveken O., Department of Ear-Nose-Throat, UZA

Research physician and contact person for more information: Department of Ear-Nose-Throat, UZA
Tel: 03 821 82 47
E-mail: eldar.tukanov@uza.be

NECESSARY INFORMATION

You are being invited to voluntarily participate in a clinical trial in which we want to use drug-induced sleep endoscopy (DISE) to investigate the effect of hypoglossal nerve stimulation (HNS) at each site of upper airway collapse.

You are being invited to participate in this study because you are eligible for treatment with HNS for obstructive sleep apnea (OSA).

You need to know the following information before participation:

- Your participation is voluntary; there can be no coercion in any way. Your signed consent is required for participation. Even after you have signed, you may inform the physician-researcher that you wish to discontinue participation. The decision whether to (further) participate or not will have no negative consequences concerning the quality of care nor the relationship with the treating physician(s).
- You will not be charged for specific visits, consultations or examinations that are part of this study.
- There is an insurance in the event that you are harmed as part of your participation in this clinical trial.
- If you would like any additional information, you can always contact the physician-investigator or a member of his or her team.

Additional information on "clinical trial participant rights" can be found in the appendix (page 5).

Study aim and description

The effect of hypoglossal nerve stimulation (HNS) on the underlying disease mechanisms of OSA still unknown. However, this is highly important for further understanding and future improvement of this therapy. Having all this information could enhance treatment and get us one step closer toward personalized treatment.

The aim of this study is to investigate the effect of HNS on the site of upper airway collapse in patients with OSA. This involves looking at observations during a clinical standard drug-induced sleep endoscopy (DISE), both before treatment and one year after treatment.
An additional aim is to investigate the effect of HNS on a new non-invasive tool - which uses a mathematic calculation on the raw sleep study (polysomnography, PSG) data to predict the location and pattern of collapses in OSA. This will allow us to investigate if this tool can be used to examine the effect of HNS on the underlying disease mechanisms of OSA.

Background information on these aims can be found in Appendix (page 5).

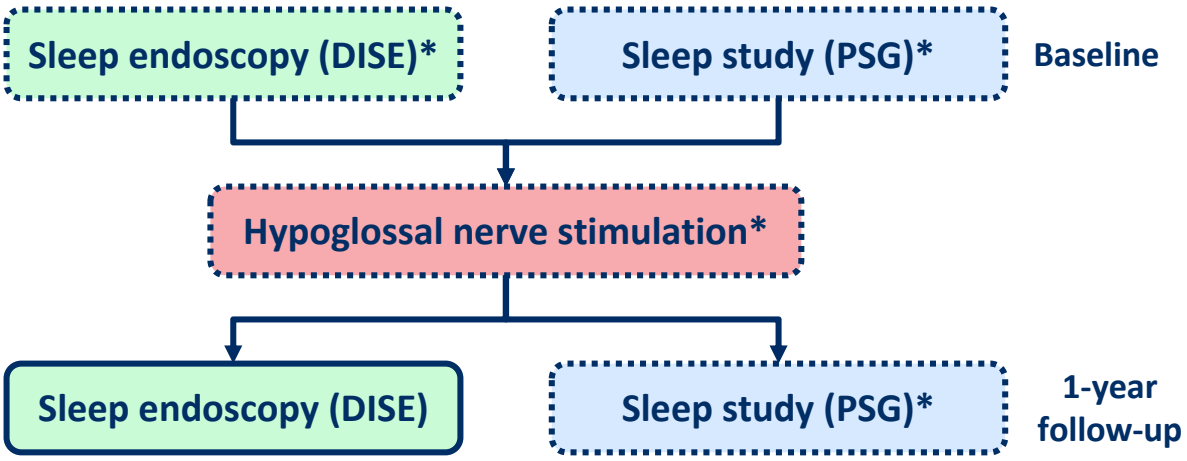
Study pathway

If you consent to the usage of your coded data in this study, data from the following investigations will be used in the study:

- The outcome of the sleep endoscopy (DISE, drug-induced sleep endoscopy). Signals as measured during the diagnostic sleep study (polysomnography, PSG).
- Clinical data relevant to your diagnosis of obstructive sleep apnea.
- The results of your treatment.

In addition, an additional DISE will be performed approximately one year after treatment with hypoglossal nerve stimulation (HNS). An overview of the course of the study can be found in Figure 1.

At all times, your data will be kept confidential and coded. Your data will be encrypted. This means that all information by which you can be identified, such as your name, date of birth and patient number, will be replaced by a study code. Which code belongs to your data will only be known by the team treating you. Consequently, you will not be identifiable by name or in any other way by anyone outside your treating team.



**: part of the standard clinical pathway for hypoglossal nerve stimulation (HNS)*
DISE: drug-induced sleep endoscopy
PSG: polysomnography

Figure 1. Interventions performed during the study. Data from these interventions will be coded and collected for usage during the study. The sleep endoscopy and sleep study before implantation (baseline) and the sleep study after one year of treatment are part of the standard pathway for hypoglossal nerve stimulation. For this specific study, you will undergo an additional sleep endoscopy after one year of treatment.

Risks and discomfort
This study will use clinical data that will be acquired during your standard clinical pathway for treatment of obstructive sleep apnea. An additional drug-induced sleep endoscopy (DISE) will be performed approximately one year after start of treatment. Therefore, possible risks and discomforts are the same as with a standard DISE procedure, consisting of nasal bleeding, laryngospasm and aspiration of saliva.

Voluntary participation
You are participation in this study is entirely voluntary and you have the right to refuse participation. Your decision whether or not to participate in this study or to discontinue your participation in the study will have no impact on your possible further treatment.

If you accept to participate in the study, you should keep this information leaflet and will be asked to sign the attached consent form.

You have the right to stop your participation in the study at any time, even after signing the consent form. You do not need to provide a reason for doing so. Withdrawing your consent will not cause any harm or loss of benefits. Your decision will not affect your further medical treatment. Nor will your decision affect your relationship with your treating physician.

Your participation in the study may also be terminated, without your consent, at any time by the physician-investigator, the Medical Ethics Committee or by the sponsor. Possible reasons for such decision may include:

- you do not comply with the instructions for participation in the study;
- your continued participation in the study is found to be harmful to you;
- it is determined during the study that you do not meet the study requirements after all.

Benefits
We cannot guarantee that if you agree to participate in this study, you will personally receive any direct benefit from your participation in this study. Given that an additional drug-induced sleep endoscopy (DISE) will be performed, there will be a better view on the effect of hypoglossal nerve stimulation on your upper airway. Information obtained from this study may contribute to a better knowledge of OSA and its treatment with hypoglossal nerve stimulation.

Protection of privacy

Your identity and your participation in this study will be kept strictly confidential. You will not be identifiable by name or through other ways in records, results or publications related to the study. The physician-investigator will encrypt your personal information so that your identity will always remain secret.

The sponsor may use your personal study data for other research purposes within the scope of this study. Only your coded information will be used for this purpose.

In accordance with Good Clinical Practice guidelines, access to your medical records will be granted to representatives of the sponsor or its affiliates and regulatory authorities, and to the extent related to the study. This is for the purpose of reviewing study data and studies and ensuring that the information is accurate.

This coded information may also be transmitted to domestic and/or foreign government agencies, to the Committee on Medical Ethics, and to other physicians and/or organizations working with the sponsor. You will not be identified by name or otherwise in records, results or publications related to the study.

Your study data will be processed and analyzed electronically (i.e., in the computer) or manually to determine the results of this study.

You have the right to ask the physician-investigator what data is being collected from you as part of the study and what purpose it has. You also have the right to ask the physician-investigator to grant you access to your personal information and to have any necessary corrections made to it. The protection of personal information is legally determined by the applicable laws and regulations on the protection of privacy.

If you agree to participate in this study, it means that you consent to the use of your coded medical information for the above purposes and to its transmission to the above-mentioned persons and/or agencies.

Contact
If you would like additional information, or in case of problems or any other concerns, you may contact the physician-investigator (Prof. Dr. O. Vanderveken) or a member of the study team (Dr. Eldar Tukanov) by phone (03 821 82 47) or e-mail (eldar.tukanov@uza.be).

If you have questions regarding your rights as a participant in the study, you may contact the ombuds service at the hospital at this telephone number: 03 821 31 60. If necessary, the ombuds service can put you in touch with the Ethics Committee.

APPENDIX

Background information on study aim

Obstructive sleep apnea (OSA) is a disease in which the upper airway repetitively narrows of even completely collapses during sleep. It is one of the most prevalent respiratory disorders and the most frequent type of sleep-disordered breathing, characterized by recurrent pharyngeal collapses during sleep. This disturbance results in recurring complete or partial collapse of the airway, called apneas and hypopneas respectively. This disruption in breathing causes reduced sleep quality and long-term adverse health effects. The diagnosis of OSA is made using a diagnostic sleep study or polysomnography (PSG). During this examination, several parameters are measured during sleep: brain activity, breathing, muscle movements of your eyes, chin and legs, heart rhythm and oxygen in the blood. These parameters allow us to diagnose sleep problems, including obstructive sleep apnea. You have already undergone this diagnostic sleep study.

As OSA is associated with multiple comorbidities, efficient treatment is mandatory. In clinical practice, the standard treatment for OSA is continuous positive airway pressure (CPAP), which opens the upper airway by providing positive pressure in the airway. Alternative treatments include mandibular advancement device (MAD) treatment, which (re)opens the upper airway by protruding the mandible, position treatment to avoid supine position, drug treatments, hypoglossal nerve stimulation treatment (the main focus of this study) and other surgical treatments. While CPAP is characterized by an overall greater efficacy, adherence might be limited. Non-CPAP treatments are characterized by a higher adherence, yet their efficacy is patient dependent.

Respiration-synchronized hypoglossal nerve stimulation (HNS) is an innovative technique in which the hypoglossal nerve is stimulated to push the tongue forward during inspiration. Patients eligible for this treatment are thoroughly selected. A drug-induced sleep endoscopy (DISE) is a reliable examination for this purpose, with a good predictive value for the effect of HNS. In fact, complete concentric collapsing of the palate (CCC) – which means that the palate is fully closed in a circular pattern – is a formal exclusion criterion for treatment with HNS worldwide.

Although DISE is a useful way to investigate the effect of HNS, it is still a time-consuming and invasive study, requiring the patient to undergo an endoscopy of the upper airway through the nose and under sedation in the operating room. Recently, a new non-invasive tool has been developed that uses raw data from a PSG to estimate the site and pattern of collapses in OSA. This tool could possibly be used to predict observations made during DISE.

While HNS treatment for OSA is applied in multiple centers across the world, the effect of HNS treatment on the underlying disease mechanisms of OSA is still unknown. However, this is highly important for further understanding and future improvement of this therapy. During this study, we aim to investigate the effect of HNS on the underlying disease mechanisms of OSA using clinical-standard DISE. We then want to compare these results between patients who respond well to HNS (responders) and patients who respond less well to HNS (non-responders). Additionally, we want to investigate the effect of HNS on the underlying disease mechanisms of OSA using a novel non-invasive tool. This way, we can investigate whether this tool can be used to examine the effect of HNS on the underlying disease mechanisms of OSA in the future.

Additional information on the protection and rights of clinical trial participants

ETHICAL COMMITTEE

This study was reviewed by the Medical Ethics Committee of the University Hospital of Antwerp. Ethics committees are tasked with protecting those who participate in clinical studies. They check whether your rights as a patient and as a study participant are respected, whether - based on current knowledge - the balance of risks and benefits is favorable to participants, and whether the study is scientifically relevant and ethical.

On this, the ethics committees issue an opinion in accordance with the Belgian law of 7 May 2004.

Under no circumstances should you consider the positive opinion of the Ethics Committees as an inducement to participate in this study.

VOLUNTARY PARTICIPATION

Do not hesitate to ask any questions that come to mind before signing. Take time to talk about them with a trusted person if you wish.

You have the right not to participate in this study or to quit this study, without having to give a reason, even if you have previously agreed to participate in this study. Your decision will in no way affect your relationship with the physician-investigator or the quality of your continued care.

If you accept to participate in this study, you will sign the consent form. The physician-investigator will also sign this form, confirming that he has given you the necessary information about this study. You will receive the copy intended for you.

It is recommended that you inform the physician-investigator if you decide to discontinue your participation in the study.

COSTS ASSOCIATED WITH YOUR PARTICIPATION

Participating in the study does not incur any additional costs for you or your insurance company. Only costs related to usual medical services may be charged to you.

CONFIDENTIALITY GUARANTEE

Your identity and your participation in this study will be kept strictly confidential. You will not be identified by name or otherwise in records, results or publications related to the study.

To guarantee your privacy regarding the storage and processing of data in the context of this study, your data will be pseudonymized. In other words, your name, first name, date of birth and place of residence will be replaced by a code. All further processing is done on this pseudonymized data. However, the link between the code and your person is preserved. This link is only used to be able to feedback certain information to you in your own interest.

If you consent to participate in this study, it means that you consent to the use of your personal data collected as part of this study.

You may withdraw consent to the collection and processing of your data at any time. If your study participation is stopped early, your original consent will allow the use of the data collected about you in relation to the period you were enrolled in the study.

Only persons directly involved in the study will have access to your personal data. Your data will not be passed on to third parties.

The researchers will retain your data for a period of 20 years. In addition, your medical data stored in your patient file at the UZA will be kept for 30 years.

You have the right to ask the researchers what data will be collected about you in the course of the study and what its purpose is. You can request that certain data be corrected or deleted or that your data no longer be used. All data collected from you will be treated in accordance with the "Directive on the protection of individuals with regard to the processing of personal data", the European General Data Protection Regulation (GDPR) (EU2016/679) and national legislation applicable to these directives.

The UZA, as the commissioner of the study, is responsible for processing your personal data. It has appointed a data processing officer for this purpose.

Questions concerning the management of your data can be addressed to the research-physician, your treating physician or to the UZA data protection officer (via e-mail: dpo@uza.be).

If you feel that your rights regarding your personal data are not sufficiently respected, you can always contact the data protection officer who will take the necessary measures if necessary. You also have the right to lodge a complaint with the Belgian Data Protection Authority.

More information can be found at https://www.uza.be/privacy.html.

INSURANCE
Any participation in a study involves a risk, however small. The project is insured for faultless liability in accordance with Article 29 of the Belgian Law of 7 May 2004 on experiments on the human person.

We therefore ask you to report any new health problem to the physician-investigator. He or she can provide you with additional information on possible treatments.

If the research-physician believes that a connection to the study is possible (there is no connection to the study in the case of injury due to the natural course of your disease or due to known side effects of your standard treatment), the sponsor of the study will be notified and a declaration procedure will be initiated with the insurance company. If necessary, an expert will be appointed to give an opinion on the link between your new health complaints and the study.

In the event of disagreement with the doctor-investigator or with the expert appointed by the insurance company, and whenever you deem it necessary, you or, in the event of your death, your beneficiaries, may sue the insurer directly in Belgium (name insurance, policy number, contact details).

INFORMED CONSENT

Study title: "Assessment of the effect of hypoglossal nerve stimulation therapy on the site of collapse during drug-induced sleep endoscopy"

Part intended for participant:

I, the undersigned …….. (name & first name),

- confirm that I have been thoroughly informed on all aspects of the project and have received a copy of the 'information folder for the study participant'. I have read and understood the information and hereby confirm my participation to the project.
- confirm that I have been given enough time to overthink my participation to the project.
- confirm that I have had the opportunity to ask questions and have received a satisfactory response.
- understand that my participation is entirely voluntary and I can withdraw at any moment, without experiencing any disadvantage.
- am willing to provide information on my medical history, medication use and enrollment in other studies. I understand that my medical data will be kept strictly confidential. I agree with the collection, analysis and use of my medical data, as described in the information folder for the study participant.

…… ……
Signature participant Date

Part intended for research team:

I confirm that I have informed the above-mentioned participant on the project and that he/she has consented with participation to the project.

……. ……. ……
Name Signature Date

INFORMED CONSENT

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…… ……
Signature participant Date

Part intended for research team:

I confirm that I have informed the above-mentioned participant on the project and that he/she has consented with participation to the project.

……. ……. ……
Name Signature Date