

A New Approach to Treating Tinnitus NeuroSystec Study

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Introduction

A new clinical study for the treatment of tinnitus using a new drug that would be directly infused into the patient's inner ear is underway. The study is conducted by the OtoRhinoLaryngology department of Avicenne Hospital (93000 Bobigny), in its Clinical Investigation Center of the hospital. The study, which includes evaluating the drug itself and its infusion device, is looking for adults who suffer from incapacitating tinnitus, in one ear, with severe or extreme hearing loss on the same side.

General description of tinnitus

Over the last few years, we have come to better understand the causes of tinnitus. Nevertheless, a wide variety of factors can cause this symptom. Here are few examples: acoustic trauma, sudden hearing loss, ototoxic drugs, direct trauma to the ear, and infections in the inner ear, etc.

Schematically, the care of patients with tinnitus follows 3 approaches:

The first is improving tolerance in several ways, with and without drugs, by offering behavioral and cognitive therapy and a habituation to the situation.

The second aims at improving hearing. In most cases tinnitus affects people with impaired hearing. Hearing is not only less efficient but it is even more unpleasant due to the tinnitus, and the closer an individual must be to a sound to hear it, the more aware they become of their tinnitus. Improving hearing is the second approach, which can be done through surgery, the use of a hearing aid, etc. The situation is more difficult when the person is profoundly or completely deaf out of the ear and cannot use an aid. To provide for an auditory sensation, we can provide electric stimulation.

The third approach is fighting against the mechanism of tinnitus itself. To explain tinnitus, there is essentially only one dominating mechanism, at least in the beginning phase: hyperactivity of the nerves in the auditory canal. It is this hyperactivity that we perceive as sound (tinnitus). For example, with acoustic trauma, it is as if there was "epilepsy" of the auditory nerve path.

Medication in the inner ear: NST 001

To combat this hyperactivity, oral medications are administered, which can cause side effects when they are effective. The side effect of an antipsychotic drug is drowsiness. This may in fact be desirable when the tinnitus is the cause of sleep disorders. But this is no longer a fight against the tinnitus mechanism rather the treatment of tolerance.

Given the complexity of its causes, the highly subjective nature of the syndrome itself, strong influence of the personal lifestyle of those who suffer from tinnitus etc., measuring the progress that can be attributed to the treatment is difficult: Clinical studies are difficult to perform. Patients must be grouped together in clinically homogenous groups: recent tinnitus, chronic tinnitus, peripheral tinnitus (mostly in the inner ear), or central tinnitus, etc. Since current medicine is based on evidence, the development of new products for tinnitus is rare.

The current study is testing a new tinnitus treatment

Research from the last 15 years has led to the discovery of new drugs which highly influence the transmission of nerve impulse. To link this back to what was said earlier, a newly found application is the hyperactivity of the nerve caused by tinnitus. A promising drug was discovered by researchers in Montpellier. In the lab, this drug (NST-001) proved to be effective on tinnitus induced in animals by "ad hoc" drugs. Thankfully, this drug did not present any dangers for human use. NeuroSystec has recently obtained approval from authorities to test this drug for *tinnitus* in France.

NST-001 was rigorously tested during safety studies and thus has been approved for its first-in-human study (Phase 1b clinical trial) by the AFSSAPS and an Ethics Committee (EC) whose responsibility is to approve the ethics of the study. This Phase 1b trial will start and be conducted at the Avicenne Hospital, under the supervision of a team of doctors who are familiar with conducting clinical trials and tinnitus treatment.

<p>The clinical study was designed to show the safety of the treatment and to determine if the drug can eliminate the perception of tinnitus.</p>
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How does this new drug work?

This new treatment will test the theory that the reduction of nerve hyperactivity caused by a lesion in the inner ear is useful to patients who suffer from severe tinnitus that is not well tolerated. The study will focus on patients in which tinnitus has recently appeared, is unilateral, combined with significant deafness, and who cannot use hearing aids to compensate.

The study will consist of infusing the drug (NST-001) directly into the inner ear (cochlea) several times a day for no more than 2 days. The study also intends to test the infusion device: A high concentration of the drug will be infused directly into the cochlea through a microscopic tube. The tube will be attached to a pump containing a syringe filled with NST-001. The tube will be surgically implanted in the cochlea, specifically, through the oval window and through its membrane (see diagram).

The patient will be under a general or local anesthetic with the eardrum in the reclining position to expose this anatomical area: the inner ear window. At the end of the two-day hospitalization, the tube will be removed. Throughout this entire tube implantation phase, the effects of the drug will be assessed through the measurement of various biological parameters and medical monitoring. Once the tube is removed and at the end of the hospitalization period, medical monitoring will take place to evaluate the long-term effects of the treatment, both the positive impact of the drugs, as well as potential side effects.

An important fact to note, which justifies this administration method, is that direct administration of this drug into the cochlea significantly reduces the amount of the drug being distributed into the body: thus, possible side effects can be minimized. In addition, the infused site in the inner ear is closed and the drug does not spread. This prevents systemic effects.

For 4 months of the study, the patient will be asked to document their observations, the severity of their tinnitus, and changes that occur. By looking at the observations from doctors and participants, it will be possible to assess the safety and efficiency of the drug. All patients will receive the drug: this is not a blind study with a placebo.

Who is sponsoring the study?

This study is organized by NeuroSystec Corporation¹, which is a pharmaceutical company in the United States that develops treatment solutions for tinnitus, that is, both the drugs and the administration devices for these drugs. NeuroSystec's objective is to develop a system that is completely implantable for the treatment of tinnitus for longer treatment with long-term benefits.

How can I benefit from this drug?

This drug is still in the research phase. A clinical study protocol for adults was approved by the health authorities in France (CPP – Committee for personal protection, AFSSAPS – French health authority). The possible benefits of the treatment will be assessed for each candidate. More information on this study will be provided to you by your doctor and the study's medical supervisors. If you can benefit from this study and wish to participate, you must sign a consent form.

If you are interested in the study, please contact Prof. Bruno Frachet. His contact information is provided below.

If you have any test results such as an audiogram, please bring them to your first visit. This will enable us to check whether you can participate in the study more quickly. The details will be presented to you and the study can start.

Conclusion:

A new approach to treating tinnitus is being developed by NeuroSystec. An anti-tinnitus drug will be infused directly into the patient's inner ear through a mini-pump for 2 days. A Phase 1b² clinical trial is being conducted at the Avicenne Hospital, in the Clinical Investigation Center – CIC). If you would like more information and would like to participate in this study, please contact:

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² Phase 1b studies are usually conducted in people to assess the half-life, absorption, distribution, biotransformation, and excretion of the drug in humans. These studies also provide a sense of the tolerance profile and harmlessness of the drug. In this case, we will also test the effects on tinnitus.

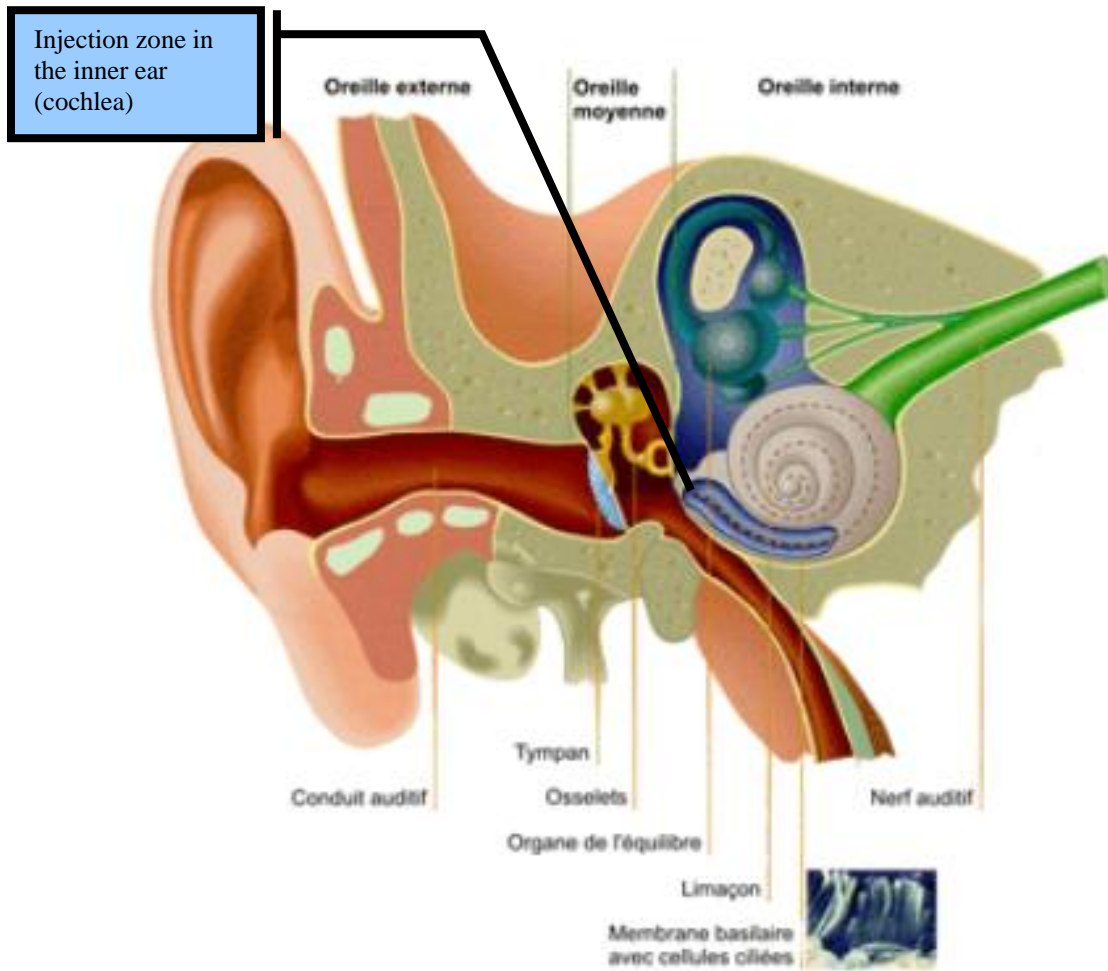
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Doctors participating in this study:

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Dr. Bertrand Geoffray, ENT
Prof. Robert Benamouzig, Head of the Clinical Investigation Center
Ms. Chery Croze, Research Director of France Acouphènes

The surgery will entail inserting a small “catheter” in the cochlea to infuse the drug.



FRENCH	ENGLISH
Oreille externe	Outer ear
Oreille moyenne	Middle ear
Oreille interne	Inner ear
Conduit auditif	Auditory canal
Tympan	Tympanic membrane (eardrum)
Osselets	Stapes
Organe de l'équilibre	Balance organ
Limaçon	Cochlea
Membrane basilaire avec cellules ciliés	Basilar membrane with ciliated cells
Nerf auditif	Auditory nerve