

Clinical Trial to Validate Drug Treatment for Acute Inner Ear Tinnitus

Carissa Joines

Kerri* was sitting in a movie theater, waiting for the film to start. As the screen flickered to life, sound unexpectedly roared to a painfully intense level. She recounts developing an intense ringing in her ears after the experience, but assumed it would go away. In the days and weeks following the onset of her tinnitus, she tried a variety of herbal and vitamin therapies to treat her condition—all without success.

Concerned that her acute tinnitus would become a permanent condition, she visited her doctor, and eventually agreed to participate in a clinical trial for AM-101, an experimental drug for acute tinnitus.

"I was getting desperate... this trial gave me hope that tinnitus wouldn't be a constant thing for me," said Kerri.

After extreme noise exposure or some other insult to the ear, acute tinnitus may set in. Oftentimes it resolves spontaneously, but in other cases acute tinnitus may develop into chronic tinnitus. (By most clinical definitions, tinnitus is considered "chronic" if conditions last longer than three to six months.)

"There is not much out there for acute tinnitus patients," says Kevin Sykes, Director of Clinical Research with the Department of Otolaryngology at the University of Kansas Medical Center, a clinical trial site. "Treatment options have been limited—mainly herbal and unproven therapies."

The investigational drug AM-101, is currently in the last stage of clinical development. The drug's developer, Auris Medical, is conducting a new clinical trial in the US to confirm the safety and efficacy that was observed in previous trials. If positive, the company intends to seek approval from the U.S. Food and Drug Administration (FDA) to market the drug.

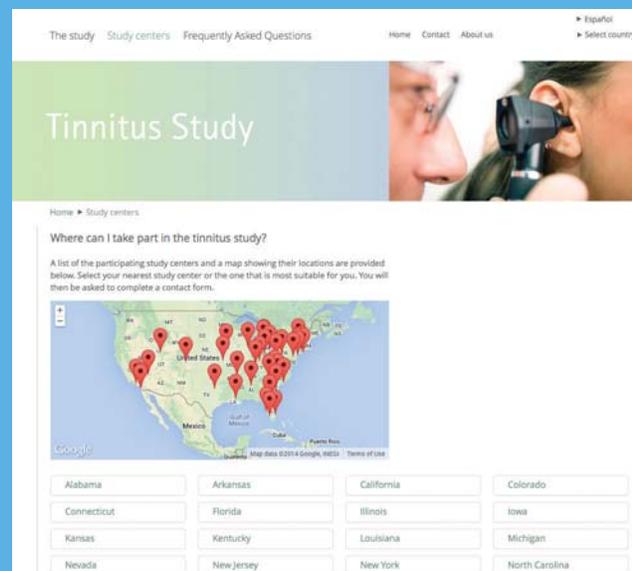
AM-101 works by inhibiting N-Methyl-D-aspartate (NMDA) receptors in the inner ear. These receptors are activated after traumatic injury to the inner ear and may be a source of the perception of tinnitus. The goal of AM-101 is to effectively treat tinnitus in its early, or acute phase, when it still originates in the ear, and before it has been centralized, or shifted, to the brain.

Preliminary data has been promising. Previous trial data showed that patients with tinnitus triggered by acute

WANT TO PARTICIPATE IN THE AM-101 TRIAL?

Researchers are looking for patients aged 18-75, who have contracted tinnitus within the past three months and have a well-documented triggering event of acoustic trauma, barotrauma, an operation on the middle ear, a traumatic perforation of the eardrum or an infection of the middle ear. There are more than 40 study sites in 22 states involved in the AM-101 trial, and more sites are being added.

For a full list of US study sites and complete participation criteria, visit www.tinnitus-study.info



The screenshot shows the "Tinnitus Study" website. At the top, there are navigation links: "The study", "Study centers", "Frequently Asked Questions", "Home", "Contact", "About us", and "Español". Below the navigation is a header with "Tinnitus Study" and a photo of a person's ear being examined. The main content area is titled "Where can I take part in the tinnitus study?" and includes a map of the United States with red pins indicating study sites. Below the map is a list of states with input fields for each state: Alabama, Arkansas, California, Colorado, Connecticut, Florida, Illinois, Iowa, Kansas, Kentucky, Louisiana, Michigan, Nevada, New Jersey, New York, and North Carolina.

*Name changed for privacy.

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noise trauma or middle ear infection, who were treated with AM-101, achieved a gradual and lasting reduction in tinnitus loudness, annoyance, and tinnitus-related sleep difficulties, as recorded by patients on numerical rating scales. In the largest trial to date, patients on average enrolled about two months after tinnitus onset and rated their tinnitus loudness before treatment at around 55 points on a 0 to 100 scale; their mean tinnitus impact on the THI-12 questionnaire was 12.2 points (moderate). Patient-reported tinnitus loudness was almost 50% lower three months after the treatment.

The therapy involves administering AM-101 by intratympanic injection—through the eardrum into the middle ear. This is a safe procedure that has been used for decades in the treatment of other ear conditions. In this quick outpatient procedure, a very small dose of the drug, about one-quarter milligram, is injected into the ear after it has been numbed. From the middle ear, the drug diffuses into the inner ear, targeting the NMDA receptors. After the treatment, the patient then must lie still for 30 minutes, allowing the drug to reach its target.

“Trial participants can go back to work the same day,” said Sandra Smith, Clinical Research Manager at Piedmont Ear, Nose, & Throat Associates in Winston-Salem, NC. “There are no residual effects, no side effects, and no scar tissue.”

Study participants receive three injections over the course of five days. Data is collected through the use of nightly patient diaries, recording the status of their tinnitus. Trial subjects also have three follow-up visits to discuss progress with a doctor, perform hearing



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tests, and answer supplemental questions.

This is a double-blind clinical trial, which includes the use of a control group receiving a placebo treatment. Neither the doctor nor the patient know if they are receiving the active drug or a placebo. Sykes says this makes some hesitant to enter the study, but most choose to participate out of the chance they will get the drug. “The use of placebo has not been a barrier to patients in my clinic,” said Sykes. “They hope to get the drug, but know that either way, they are contributing to the knowledge on tinnitus.”

Researchers make no claim that AM-101 is a tinnitus cure. But the investigatory drug may minimize the intensity and duration of acute tinnitus symptoms. Study investigators have stated their participants report their tinnitus is less noticeable, less intense and annoying, and less

frequent after treatment. Sleep difficulties associated with tinnitus were also decreased.

For patients like Kerri, AM-101 may also be an early intervention treatment that prevents acute tinnitus from developing into a lifelong case of chronic tinnitus.

“Thus far, we have found no serious adverse events or significant side effects in patients,” concluded Sykes. “There is a fair level of confidence that this is will be a low risk and effective intervention for acute tinnitus.”

Editor's Note: Auris Medical is a Gold-Level Corporate Member of the American Tinnitus Association