Keyzilen® (AM-101) for Acute Inner Ear Tinnitus

Esketamine hydrochloride otic gel for intratympanic use

Auris Medical
Cochlear therapies

About Keyzilen® (AM-101)

Keyzilen® contains the N-methyl-D-aspartate (NMDA) receptor antagonist esketamine formulated in a biocompatible, fully biodegradable gel that targets aberrant excitation of the auditory nerve, which is at the origin of certain types of tinnitus.

Keyzilen® is being developed for the treatment of acute inner ear tinnitus following traumatic cochlear injury or otitis media and is delivered locally into the middle ear by an otolaryngologist (ear, nose, throat physician) through intratympanic administration. AM-101 0.87 mg/mL is administered three times over three to five days.

In Phase 2 clinical trials, Keyzilen® was well tolerated and showed dose-dependent and persistent improvements in tinnitus loudness and other outcomes. Keyzilen® has Fast Track designation from the US Food & Drug Administration.

Phase 3 Clinical Trials

The Phase 3 clinical development program for Keyzilen® includes two placebo-controlled trials: the TACTT2 trial conducted primarily in North America and the TACTT3 trial conducted in Europe.

Top-line results from the TACTT2 trial were announced in August 2016. Although the trial did not meet its co-primary efficacy endpoints, the data show greater improvements as compared to placebo in the Tinnitus Functional Index (TFI) for active-treated patients who suffered from tinnitus following otitis media and who suffered from severe or extreme tinnitus at baseline.

Based on the results from TACTT2, Auris Medical amended the TACTT3 trial while still fully blinded to its results. Under the amendment, the TFI was elevated from a key secondary endpoint to an alternate primary endpoint, the subgroups of patients with tinnitus following otitis media and patients with severe or extreme tinnitus were included in confirmatory testing and additional patients are enrolling in the trial. Auris Medical expects to announce top-line results from the expanded trial in the first quarter of 2018.

Phase 3 trial participants were presented the option to roll over into open-label studies (AMPACT1 and AMPACT2) and receive additional treatment cycles. Results from these studies confirm the long-term safety of Keyzilen®. In addition, exploratory efficacy analyses further support early treatment from onset of inner ear tinnitus and suggest potential benefits of repeating treatment cycles.

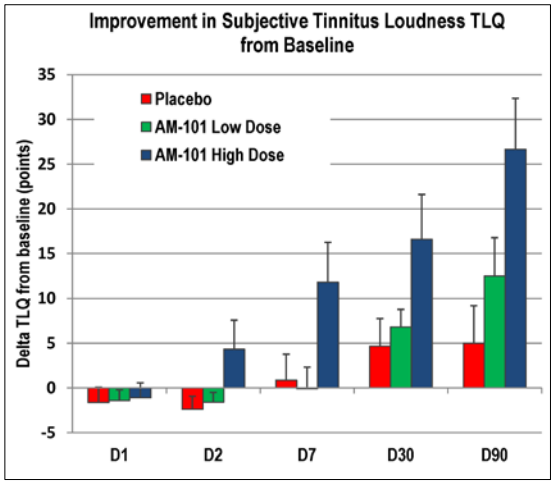
Phase 2 Clinical Trials

Auris Medical conducted two randomized, placebo-controlled Phase 2 trials enrolling 248 (TACTT0) and 85 (TACTT1) patients with acute inner ear tinnitus following acute acoustic trauma or otitis media. In TACTT0, AM-101 0.27 or 0.81 mg/mL or placebo was administered three times over three consecutive days, while in TACTT1, AM-101 0.81 mg/mL or placebo was administered either in a single dose or three times over two weeks.

TACTT0 Efficacy: Patients treated with AM-101 0.81 mg/mL showed a gradual and statistically significant improvement to Day 90 in tinnitus loudness (co-primary endpoint), sleep difficulties and overall tinnitus impact over placebo. At Day 90, mean tinnitus loudness improved by 48%; 62% of patients (unilaterally affected and treated) reported much or very much improved tinnitus severity.

TACTT1 Efficacy: Patients showed the same type of improvement in tinnitus loudness and other outcomes over placebo as in TACTT0. Trends for 1 x AM-101 and 3 x AM-101 were similar.

Safety: Keyzilen® was well tolerated and had no negative impact on hearing. Adverse events were mostly local and procedure-related. A number of patients experienced a transient increase in tinnitus loudness and muffled hearing. These effects usually resolved with closure of the eardrum (typically a few days following injection).



Mean absolute improvement of subjective tinnitus loudness (TLQ) from baseline in patients with unilateral tinnitus following acute acoustic trauma or otitis media (n = 84). TLQ was rated on a scale from 0 (no tinnitus heard) to 100 (extremely loud). Study participants received three injections of AM-101 or placebo on Day 0, Day 1 and Day 2. Error bars represent standard error of the mean. Van de Heyning et al., 2014.