AM-111 for Acute Inner Ear Hearing Loss

Brimapitide otic gel for intratympanic use

Auris Medical
Cochlear therapies

About AM-111

AM-111 contains brimapitide, or D-JNKI-1, an inhibitor of the JNK stress kinase coupled to an intracellular transporter. AM-111 is formulated in a biocompatible and fully biodegradable gel and administered in a single dose via intratympanic administration locally into the middle ear by an otolaryngologist (ear, nose, throat physician). AM-111 blocks cell death (apoptosis) in stress-injured sensory cells and attenuates inflammation after acute inner ear injury.

AM-111 has orphan drug designation from both the US Food & Drug Administration and the European Medicines Agency for the treatment of acute sensorineural hearing loss (ASNHL): hearing loss from acoustic trauma, sudden deafness (idiopathic sudden sensorineural hearing loss; ISSNHL) and surgery-induced acoustic trauma. In addition, the FDA has granted AM-111 fast track designation.

Phase 2 Clinical Trial

In a randomized, placebo-controlled Phase 2 trial of 210 patients who suffered from either ASNHL following acute noise trauma or ISSNHL, patients were treated within 48 hours post-onset with a single dose of AM-111 0.4 mg/mL, 2.0 mg/mL or placebo. The primary endpoint of the trial was the recovery in hearing between baseline and Day 7.

Efficacy: Patients with severe to profound hearing loss (i.e. hearing thresholds ≥ 60 dB at the three worst affected test frequencies) who were treated with AM-111 0.4 mg/mL showed a clinically relevant improvement in hearing threshold and speech discrimination and a higher rate of complete tinnitus remission compared with placebo. Hearing thresholds improved by 29.9 dB at Day 7 and 44.3 dB at Day 90 in the active group compared with 17.9 dB and 33.5 dB in the placebo group, respectively. Improvement in the AM-111 2.0 mg/mL group tended to be lower and failed to reach significance.

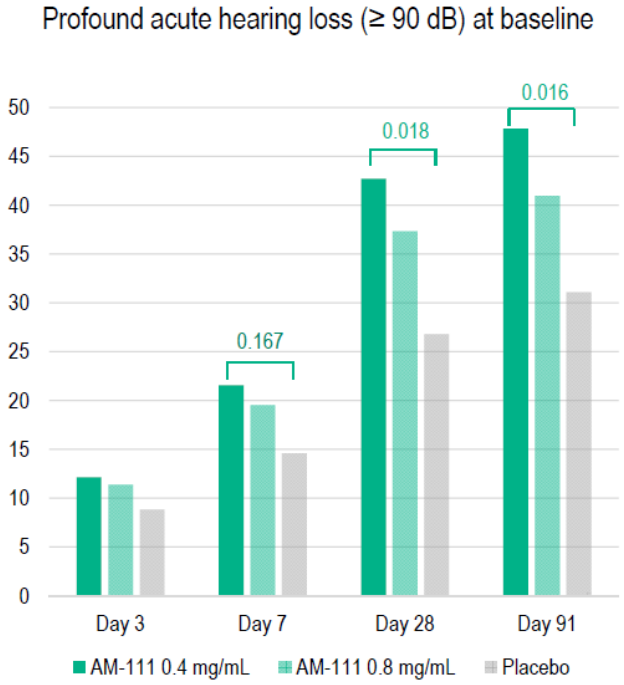
Safety: AM-111 was well tolerated with no negative impact on hearing, balance or tinnitus. Adverse events were mostly local, transient and procedure-related, such as ear discomfort, incision-site complications, or middle ear infection in less than 5% of patients.

Phase 3 Clinical Development

The HEALOS Phase 3 trial was conducted in Europe and Asia and enrolled 256 patients suffering from severe to profound acute hearing loss within 72 hours of ISSNHL onset.

Patients were treated with a single dose of AM-111 0.4 mg/mL, 0.8 mg/mL or placebo. The primary endpoint of the trial was the hearing recovery from baseline to Day 28.

Efficacy: The primary efficacy endpoint was not met in the overall population. A post-hoc analysis of patients with profound acute hearing loss (i.e. hearing threshold ≥ 90 dB at baseline) revealed a clinically and statistically significant improvement in the AM-111 0.4 mg/mL treatment group. Hearing improved at Day 28 by 42.7 dB in the AM-111 0.4 mg/mL group vs. 26.8 dB in the placebo group (p=0.0176). Active-treated patients also showed a statistically significantly lower incidence of no hearing improvement compared to placebo by Day 91 (11.4 vs. 38.2%, risk ratio 0.30, p=0.012). In addition, their word recognition score increased substantially more (49.2 vs. 30.4 percentage points; p=0.062).



Improvement of hearing threshold at the average of the three worst affected contiguous test frequencies from baseline; post-hoc repeated measures ANCOVA (mITT; n=98).

Safety: AM-111 was well tolerated and the primary safety endpoint was met, i.e. there was no difference in the occurrence of clinically relevant hearing deterioration between the treatment groups at Day 28.

In a next step, the Company will seek to discuss the regulatory pathway based on the data from HEALOS and also the ASSENT trial, which was terminated early.