Extract of Final Study Report:

A Phase III multicentre, double-blind, placebo-controlled, study evaluating the safety, and efficacy of STR001 treatment in adults with Sudden Sensorineural Hearing Loss.

Date 27-July-2020

Pages 60-63

11.4.3 Analysis of Efficacy

11.4.3.1 Average Hearing Improvement (AHI) after 12 Weeks Measured with PTA

Average hearing improvement (AHI) are summarized by treatment and visit including change from baseline in Tables 14.2.4.1.1 (ITT) and 14.2.4.1.2 (PP).

On ITT population, the geometric LS mean of AHI for STR-5 group and Placebo group at Week 12 was 42.3 dB and 41.2 dB, respectively. No statistically significant differences were observed in AHI values between STR-5 group and Placebo group (p=0.8537) (Table 11-4). Similarly, no statistically significant differences were observed in AHI values between STR-0 group and Placebo group (p=0.4225) (Table 11-5).

Table 11-4 Summary of ANCOVA Model for AHI at Week 12 for STR-5 vs. Placebo (Intent-To-Treat Population)

			STR-5		Placebo		GMR			
Comparison	Time Point	Test (Unit)	N	Geo LS Means	N	Geo LS Means	Estimate	95% CI	CV	P-value
STR-5 vs. Placebo	Visit 6 (Week 12)	AHI (dB)	49	42.3	49	41.2	1.03	(0.77 ; 1.36)	52.64	0.8537

AHI: Average hearing improvement; CV: coefficient of variation; Geo: Geometric; GMR: Geometric means ratio; LS: Least squares; N: number of patient with evaluable response; Placebo: Intratympanic placebo treatment and placebo tablets; STR-5: Intratympanic STR treatment and STR tablets.
Source: Table 14.2.4.7.1 and Appendix 16.1.9.1.1

Table 11-5 Summary of ANCOVA Model for AHI at Week 12 for STR-0 vs. Placebo (Intent-To-Treat Population)

			STR-0		Placebo		GMR			
Comparison	Time Point	Test (Unit)	N	Geo LS Means	N	Geo LS Means	Estimate	95% CI	CV	P-value
STR-0 vs. Placebo	Visit 6 (Week 12)	AHI (dB)	50	37.6	49	41.3	0.91	(0.73; 1.15)	44.67	0.4225

AHI: Average hearing improvement; CV: coefficient of variation; Geo: Geometric; GMR: Geometric means ratio; LS: Least squares; N: number of patient with evaluable response; Placebo: Intratympanic placebo treatment and placebo tablets; STR-0: Intratympanic STR treatment and placebo tablets.
Source: Table 14.2.4.9.1 and Appendix 16.1.9.3.1

Proportion of improvement in AHI is summarized by treatment group and visit in Tables 14.2.4.19.1 (ITT) and 14.2.4.19.2 (PP). Summary of analysis of covariance (ANCOVA) Model for AHI at 12 Weeks for pooled STR vs. Placebo group is presented in Tables 14.2.4.27.1 (ITT) and Table 14.2.4.27.2 (PP). No statistically significant differences were observed between pooled STR and Placebo group.

Summary of paired t-test results for AHI scores for STR-5 group between Week 12 and Week 24 is presented in Tables 14.2.4.16.1 (ITT) and 14.2.4.16.2 (PP). Statistically significant differences were observed in AHI scores between Week 12 and Week 24 (ITT: p= 0.0003, PP: p=0.0005). The results suggested that there was a further improvement in hearing for all treatment groups between week 12 and week 24 without treatment.

11.4.3.2 Analysis of Secondary Efficacy Variables

11.4.3.2.1 Speech Recognition Improvement after 12 and 24 Weeks

Individual result of speech recognition assessment are listed by patient and visit in Listing 16.2.6.2. Results of speech recognition are summarized by treatment, language and visit including change from baseline in Tables 14.2.4.2.1 (ITT) and 14.2.4.2.2 (PP).

Improvement in speech recognition at 60 dB in STR-5 and Placebo groups at Week 12 was 41.3% and 40.0%, respectively. No statistically significant differences were observed between STR-5 group and Placebo group. Similarly, no statistically significant differences were observed in improvement in speech recognition at 80 dB between STR-5 group and Placebo group at Week 12 (Table 11-6).

No statistically significant differences were observed between STR-0 group and Placebo group in improvement in speech recognition at 60 dB at Week 12. Differences were observed between STR-0 group and Placebo group in improvement in speech recognition at 80 dB at Week 12 (p=0.0422) (Table 11-7). Due to the stepwise approach used to maintain the overall alpha level for the study this result is not considered statistically significant.

Table 11-6 Summary of ANCOVA Model for Speech Recognition at Week 12 for STR-5 vs. Placebo (Intent-To-Treat Population)

				LSMeans				
Comparison	**Time Point**	**Test (Unit)**	**N**	**STR-5**	**Placebo**	**Difference (Test - Reference)**	**95% Confidence Interval of Difference**	**Std. Dev.**	**P-value**
STR-5 vs. Placebo	Visit 6 (Week 12)	Improvement in Speech Recognition at 60 dB (%)	100	41.3	40.0	1.28	(-15.44; 18.00)	29.61	0.8796
		Improvement in Speech Recognition at 80 dB (%)	99	29.0	30.4	-1.44	(-18.02; 15.13)	28.53	0.8629

Only the affected ear is considered in the analysis.
LS: Least squares; N: number of patients with evaluable response; Placebo: Intratympanic placebo treatment and placebo tablets; Std. Dev.: standard deviation; STR-5: Intratympanic STR treatment and STR tablets.
Source: Table 14.2.4.8.1 and Appendix 16.1.9.2.1

Table 11-7 Summary of ANCOVA Model for Speech Recognition at Week 12 for STR-0 vs. Placebo (Intent-To-Treat Population)

				LSMeans				
Comparison	**Time Point**	**Test (Unit)**	**N**	**STR-0**	**Placebo**	**Difference (Test - Reference)**	**95% Confidence Interval of Difference**	**Std. Dev.**	**P-value**
STR-0 vs. Placebo	Visit 6 (Week 12)	Improvement in Speech Recognition at 60 dB (%)	99	29.7	40.9	-11.25	(-25.22; 2.72)	26.06	0.1129
		Improvement in Speech Recognition at 80 dB (%)	100	17.5	31.4	-13.86	(-27.23; -0.50)	25.06	0.0422

Only the affected ear is considered in the analysis.
N: number of patient with evaluable response; Placebo: Intratympanic placebo treatment and placebo tablets; Std. Dev.: standard deviation; LS: Least squares; STR-0: Intratympanic STR treatment and placebo tablets..
Source: Table 14.2.4.10.1 and Appendix 16.1.9.4.1