Clinical trial results:
A Phase III multicenter, double-blind, placebo-controlled, study evaluating the safety, and efficacy of STR001 treatment (intratympanic injection + tablets) in adults with Sudden Sensorineural Hearing Loss

Summary

EudraCT number	2017-000242-22
Trial protocol	DE CZ PL
Global end of trial date	06 February 2020

Results information

Result version number	v1 (current)
This version publication date	10 September 2020
First version publication date	10 September 2020
Summary attachment (see zip file)	STR001-202_Statistical Analysis of Efficacy of Primary and Key Secondary Endpoints (STR001-202_Statistical Analysis of Efficacy of Primary and Key Secondary Endpoints.pdf)

Trial information

Trial identification

Sponsor protocol code	STR001-202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Strekin AG
Sponsor organisation address	Hochbergerstrasse 60C, Basel, Switzerland, 4057
Public contact	Alexander Bausch, PhD CEO, Strekin AG, +41 797888252, alexander.bausch@strekin.com
Scientific contact	Viktor Boerlin, MD Chief Medical Officer, Strekin AG, +41 791267335, viktor.boerlin@strekin.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 July 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 February 2020
Global end of trial reached?	Yes
Global end of trial date	06 February 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study are:
- To evaluate the safety and tolerability of intratympanic administration of STR001-IT thermogel followed by oral treatment with STR001-ER in patients with Sudden Sensorineural Hearing Loss
- To assess the efficacy of intratympanic administration of STR001-IT thermogel followed by oral treatment with STR001-ER in measuring hearing improvement at week 12 by PTA measurement at the 3 most contiguous affected frequencies seen at baseline

Protection of trial subjects:

Study reviewed by independent ethics committees in all countries according to regulations. Subjects were treated within the usual settings in participating sites or were referred to them by practising ENT physicians.

Background therapy:

All patients received the local standard of care for sudden sensorineural hearing loss, including a corticosteroid preparation.

Evidence for comparator:

The comparison for STR001 intratympanic injection and STR001 tablets were placebo formulations. No generally approved drug for the treatment of sudden sensorineural hearing loss is available.

Actual start date of recruitment	01 June 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 18
Country: Number of subjects enrolled	Czech Republic: 18
Country: Number of subjects enrolled	Germany: 29
Country: Number of subjects enrolled	Russian Federation: 84
Country: Number of subjects enrolled	Switzerland: 16
Worldwide total number of subjects	165
EEA total number of subjects	65

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	126
From 65 to 84 years	39
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period: 01-06-2017 to 06-12-2019 in 5 countries: Czech Republic, Germany, Poland, Russian Federation and Switzerland. First patient randomized on 24-10-2017.

Pre-assignment

Screening details:

Patients were recruited when they had noticed severe sudden hearing loss and contacted one of the participating sites or were referred to them by a ear-nose-throat doctor in practice. The patients had an audiogram and when the diagnosis of severe or profound sudden sensorineural hearing loss was confirmed, they were candidates for the study

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Data analyst, Carer, Assessor, Subject

Blinding implementation details:

Since active and placebo suspension in the ampoules did not have exactly the same appearance, the syringe was prepared by an independent study site person and handed with a cover to the injecting investigator. The active and placebo tablets were of identical appearance and were distributed to the patients in bottles.

Arms

Are arms mutually exclusive?	Yes
Arm title	STR-5: Active Treatment

Arm description:

Patients randomized to Arm 1 received an intratympanic injection of STR001 at Day 1 and underwent a 3-month oral treatment with STR001 tablets

Arm type	Experimental
Investigational medicinal product name	STR001 thermogel and STR001-ER (tablets)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion, Tablet
Routes of administration	Auricular use, Oral use

Dosage and administration details:

On Day 1 all patients in Arm1 received an intratympanic injection of STR001 thermogel. For the following three months the patients were provided with STR001 tablets containing 5 mg of pioglitazone once daily.

Arm title	STR-0: STR001 intratympanic injection + placebo tablets

Arm description:

Patients in Arm 2 received an intratympanic injection of STR001 at Day1, For the following three months they received one placebo tablet per day.

Arm type	Experimental
Investigational medicinal product name	Placebo tablets
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

All patients received at Day 1 an intratympanal injection of STR001. For the following three months they received one tablet of placebo per day.

Arm title	Placebo

Arm description:

Patients in Arm 3 received an intratympanic injection of placebo at Day 1 and for the following three months a placebo tablet per day.

Arm type	Placebo
Investigational medicinal product name	Placebo injection solution and placebo tablets
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection, Tablet
Routes of administration	Intratympanic use , Oral use

Dosage and administration details:

On Day 1 all patients in Arm3 received an intratympanic injection of placebo thermogel. For the following three months the patients were provided with placebo tablets once daily.

Number of subjects in period 1	STR-5: Active Treatment	STR-0: STR001 intratympanic injection + placebo tablets	Placebo
Started	56	56	53
Completed	50	52	50
Not completed	6	4	3
Consent withdrawn by subject	3	1	2
Subject not dosed	-	-	1
Adverse event, non-fatal	-	1	-
patient randomized but not dosed	1	-	-
Lost to follow-up	2	1	-
Physician's decision	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	STR-5: Active Treatment
Reporting group description:	
Patients randomized to Arm 1 received an intratympanic injection of STR001 at Day 1 and underwent a 3-month oral treatment with STR001 tablets	
Reporting group title	STR-0: STR001 intratympanic injection + placebo tablets
Reporting group description:	
Patients in Arm 2 received an intratympanic injection of STR001 at Day1, For the following three months they received one placebo tablet per day.	
Reporting group title	Placebo
Reporting group description:	
Patients in Arm 3 received an intratympanic injection of placebo at Day 1 and for the following three months a placebo tablet per day.	

Reporting group values	STR-5: Active Treatment	STR-0: STR001 intratympanic injection + placebo tablets	Placebo
Number of subjects	56	56	53
Age categorical			
Subjects enrolled per age group			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	43	44	42
From 65-84 years	13	12	11
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	30	32	31
Male	26	24	22

Reporting group values	Total		
Number of subjects	165		
Age categorical			
Subjects enrolled per age group			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		

Adolescents (12-17 years)	0		
Adults (18-64 years)	129		
From 65-84 years	36		
85 years and over	0		
Gender categorical Units: Subjects			
Female	93		
Male	72		

Subject analysis sets

Subject analysis set title	Intention-to-treat
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Includes all randomized patients

Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

Includes patients who have received at least one dose of study drug.

Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:

Patients who completed the trial according to the protocol without major protocol violations influencing the efficacy results.

Reporting group values	Intention-to-treat	Safety Set	Per Protocol Set
Number of subjects	165	162	134
Age categorical			
Subjects enrolled per age group			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	129	124	104
From 65-84 years	36	38	30
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	93	83	70
Male	72	79	64

End points

End points reporting groups

Reporting group title	STR-5: Active Treatment
Reporting group description:	
Patients randomized to Arm 1 received an intratympanic injection of STR001 at Day 1 and underwent a 3-month oral treatment with STR001 tablets	
Reporting group title	STR-0: STR001 intratympanic injection + placebo tablets
Reporting group description:	
Patients in Arm 2 received an intratympanic injection of STR001 at Day1, For the following three months they received one placebo tablet per day.	
Reporting group title	Placebo
Reporting group description:	
Patients in Arm 3 received an intratympanic injection of placebo at Day 1 and for the following three months a placebo tablet per day.	
Subject analysis set title	Intention-to-treat
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Includes all randomized patients	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
Includes patients who have received at least one dose of study drug.	
Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol
Subject analysis set description:	
Patients who completed the trial according to the protocol without major protocol violations influencing the efficacy results.	

Primary: Absolute hearing improvement using average pure tone audiogram thresholds

End point title	Absolute hearing improvement using average pure tone audiogram thresholds[1]
End point description:	
Improvement of absolute hearing measured as the average of the three most affected contiguous frequencies using pure tone audiometry.	
End point type	Primary
End point timeframe:	
Baseline to Week 12	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The statistical analysis was planned in two steps: firstly the comparison of STR-5 and placebo for the endpoints, secondly the comparison of STR-0 and placebo. Details are in the attachment

End point values	STR-5: Active Treatment	STR-0: STR001 intratympanic injection + placebo tablets	Placebo	Intention-to-treat
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	53	53	50	156
Units: dB				
arithmetic mean (standard deviation)	45 (± 21)	40 (± 17)	44 (± 18)	43 (± 19)

Statistical analyses

No statistical analyses for this end point

Secondary: Improvement of speech recognition at 60 dB

End point title	Improvement of speech recognition at 60 dB
End point description: Improvement in the percentage of 20 words in local language at 60dB understood	
End point type	Secondary
End point timeframe: From Baseline to Week 12	

End point values	STR-5: Active Treatment	STR-0: STR001 intratympanic injection + placebo tablets	Placebo	Intention-to-treat
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	51	50	50	151
Units: words understood	38	40	40	39

Statistical analyses

No statistical analyses for this end point

Secondary: Improvement in speech recognition at 80 dB

End point title	Improvement in speech recognition at 80 dB
End point description: Improvement in the percentage of words out of 20 in local language understood at 80 dB	
End point type	Secondary
End point timeframe: Baseline to Week 12	

End point values	STR-5: Active Treatment	STR-0: STR001 intratympanic injection + placebo tablets	Placebo	Intention-to-treat
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	50	51	50	151
Units: words understood	29	28	28	28

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Patients were followed for 24 Weeks after randomization. After Week 12, the patients did not receive any study medication.

Adverse event reporting additional description:

Advere events were collected from patient reporting, physical findings and laboratory results.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20

Reporting groups

Reporting group title	STR-5

Reporting group description:

See description in the results section:
STR001 intratympanic injection at Day1 followed by three months oral tablet treatment with 5 mg of STR001.

Reporting group title	STR-0

Reporting group description:

Patients in this treatment group received at Day 1 an intratympanic injection of STR001, followed by three months once daily intake of a placebo tablet.

Reporting group title	Placebo

Reporting group description:

Patients received at Day 1 an intratympanic injection of placebo followed by a three months oral administration of placebo tablets once daily.

Serious adverse events	STR-5	STR-0	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 54 (0.00%)	0 / 56 (0.00%)	0 / 52 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	STR-5	STR-0	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 54 (27.78%)	21 / 56 (37.50%)	15 / 52 (28.85%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 54 (3.70%)	7 / 56 (12.50%)	2 / 52 (3.85%)
occurrences (all)	2	7	2

Headache			
subjects affected / exposed	6 / 54 (11.11%)	1 / 56 (1.79%)	6 / 52 (11.54%)
occurrences (all)	6	1	6
Ear and labyrinth disorders			
Tinnitus	Additional description: Tinnitus can be a symptom of sudden sensorineural hearing loss. Whether tinnitus was caused by the disease to study or the study drug cannot be determined.3		
subjects affected / exposed	3 / 54 (5.56%)	7 / 56 (12.50%)	1 / 52 (1.92%)
occurrences (all)	3	7	1
Vertigo	Additional description: Vertigo may be a symptom of sudden sensorineural hearing loss. Whether patients' vertigo was caused by administration of the study drug or by the disease to study could not be determined.		
subjects affected / exposed	1 / 54 (1.85%)	5 / 56 (8.93%)	4 / 52 (7.69%)
occurrences (all)	1	6	4
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 54 (5.56%)	1 / 56 (1.79%)	2 / 52 (3.85%)
occurrences (all)	3	1	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 February 2018	Amendment 1 - substantial - Change and clearer description of secondary study objectives - Increase in severity of hearing loss from average pure tone audiometric threshold from 60 dB to 75 dB. Change in inclusion criterion 4. - Removal of exclusion criterion 2: no upper limit of hearing threshold defined. - Change in exclusion criterion 5: definition of air-bone gap in the most affected frequencies at baseline. - Amendment of protective measures for contraception - Change in storage condition requirement for study drug tablets - Addition of hyperbaric oxygen therapy among the prohibited treatments during study - Restriction of time frame to one month prior baseline for capturing medications in the eCRF - Change for guidance in microscopic urinalysis (only if positive findings with dipstick) - Reduction of blood safety parameters to be analysed - Change in BCTA frequency assessment - Plan for blinded interim analysis (not conducted eventually) - Minor change in schedule of assessments
05 July 2019	Amendment 2 - considered administrative amendment Change affected the timepoint of a blinded interim analysis for the primary endpoint. It was moved to the time when all patients had reached the Week 12 visit and terminated study treaments. This analysis was performed by an independent statistician and the study team were kept blinded with regard to individual data.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The template did not allow to enter the statistical analyses data. Therefore they will be supplied by a summary attachment of the statistical analyses for the primary and the key secondary endpoint.

Notes: