Clinical trial results:
A Phase II multicenter, placebo-controlled, proof-of-concept study evaluating the safety, and efficacy of intratympanic STR001 thermogel to preserve residual hearing in adults undergoing cochlear implant surgery

Summary

EudraCT number	2015-002672-25
Trial protocol	DE ES IT
Global end of trial date	15 November 2017

Results information

Result version number	v1 (current)
This version publication date	25 September 2019
First version publication date	25 September 2019

Trial information

Trial identification

Sponsor protocol code	STR001-201

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	CEO, Strekin AG, 0041 797888252, Alexander.bausch@strekin.com
Scientific contact	CEO, Strekin AG, 0041 797888252, Alexander.bausch@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	22 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 November 2017
Global end of trial reached?	Yes
Global end of trial date	15 November 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of STR001 thermogel in patients receiving cochlear implants
To assess the efficacy of STR001 thermogel in preserving hearing 6 weeks after cochlear implant surgery as determined by average Pure Tone Audiometry (aPTA) values

Protection of trial subjects:

Study reviewed by idependent ethics committees in all countries according to regulations. Subjects were treated within the usual setting and procedure of receiving a cochela implant surgery. In order to keep the potential adverse events of a local intratympanic injection lowest possible, the patient was put in a lying position and the study drug thermogel was put on body temperature before administration.

Background therapy:

All patients eligible for the study were candidates to receive a cochlea implant surgery.

Evidence for comparator: -

Actual start date of recruitment	25 January 2015
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	Spain: 26
Country: Number of subjects enrolled	France: 16
Country: Number of subjects enrolled	Germany: 66
Country: Number of subjects enrolled	Italy: 2
Worldwide total number of subjects	110
EEA total number of subjects	110

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	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)	81
From 65 to 84 years	29
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period: 25-Jan-2015 to 06-Oct-2017 in 4 countries: Germany, France, Italy and Spain

Pre-assignment

Screening details:

Patients were eligible for the study, if they had a moderate to severe hearing loss and were candidates to receive a cochlea implant surgery. No other specific screening details were required in 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	Subject, Investigator, Monitor, Carer, Assessor

Blinding implementation details:

Since active and placebo suspension did not have the same appearance the syringe was prepared by an unblinded study site personnel and handed over with a cover (foil) to the investigator for study drug application.

Arms

Are arms mutually exclusive?	Yes
Arm title	Active Treatment

Arm description:

Receiving STR001 thermogel drug substance as an intratympanic injection

Arm type	Experimental
Investigational medicinal product name	STR001 Thermogel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersion for injection/infusion
Routes of administration	Auricular use

Dosage and administration details:

STR001 1.2% Thermogel for application of 1ml as an intratympanal injection

Arm title	Placebo

Arm description:

Receiving STR001 Placebo Thermogel for intratympanic injection

Arm type	Placebo
Investigational medicinal product name	STR001 Placebo Thermogel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Auricular use

Dosage and administration details:

STR001 Placebo Thermogel for 1mL intratymanal injection of study drug

Number of subjects in period 1	Active Treatment	Placebo
Started	55	55
Completed	55	55

Baseline characteristics

Reporting groups	
Reporting group title	Active Treatment
Reporting group description:	
Receiving STR001 thermogel drug substance as an intratympanic injection	
Reporting group title	Placebo
Reporting group description:	
Receiving STR001 Placebo Thermogel for intratympanic injection	

Reporting group values	Active Treatment	Placebo	Total
Number of subjects	55	55	110
Age categorical 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	38	81
From 65-84 years	12	17	29
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	33	27	60
Male	22	28	50

Subject analysis sets	
Subject analysis set title	ITT Analysis
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Includes all randomised patients. ITT patients will be analysed in the treatment group they were randomized to, regardless of the treatment they may have received.	

Reporting group values	ITT Analysis		
Number of subjects	110		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years)			

Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over	 81 29 		
Gender categorical Units: Subjects			
Female Male	60 50		

End points

End points reporting groups

Reporting group title	Active Treatment
Reporting group description:	
Receiving STR001 thermogel drug substance as an intratympanic injection	
Reporting group title	Placebo
Reporting group description:	
Receiving STR001 Placebo Thermogel for intratympanic injection	
Subject analysis set title	ITT Analysis
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Includes all randomised patients. ITT patients will be analysed in the treatment group they were randomized to, regardless of the treatment they may have received.	

Primary: Pure Tone Audiometry Threshold of the implanted ear as the average (aPTA) of the following frequencies: 125, 250, 500 and 750 Hz at Week 6

End point title	Pure Tone Audiometry Threshold of the implanted ear as the average (aPTA) of the following frequencies: 125, 250, 500 and 750 Hz at Week 6
End point description:	
To assess the efficacy of STR001 thermogel in preserving hearing 6 weeks after cochlear implant surgery as determined by average Pure Tone Audiometry (aPTA) values	
End point type	Primary
End point timeframe:	
Baseline - week 6	

End point values	Active Treatment	Placebo	ITT Analysis	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	53	54	107	
Units: PTA Threshold				
arithmetic mean (standard deviation)	25 (± 16)	27 (± 16)	26 (± 16)	

Attachments (see zip file)	Efficacy chart for result posting.JPG

Statistical analyses

Statistical analysis title	aPTA (average pure tone audiometry threshold)
Statistical analysis description:	
Descriptive statistics and change from baseline to Week 6, were performed on PTA values for original imputation method (no significant treatment effect favouring STR001 was detected, no conservative analysis performed)	

Comparison groups	Placebo v Active Treatment

Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 5
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	10.5
Confidence interval	
level	95 %
sides	1-sided
lower limit	10.5
Variability estimate	Standard deviation
Dispersion value	20

Notes:

[1] - The average postoperative hearing loss was in the same range for both treatment arms. For the STR001 arm the average hearing loss was 25±16 dB while for the placebo arm the average hearing loss was 27±16 dB. The nominal difference between the two groups was not statistically significant. The primary study objective was not met.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline - week 6

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19

Reporting groups

Reporting group title	Active Treatment STR001
Reporting group description: -	
Reporting group title	Placebo Treatment Group

Reporting group description: -

Serious adverse events	Active Treatment STR001	Placebo Treatment Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 53 (1.89%)	3 / 55 (5.45%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
admission to other hospital due to Suspected Acute Coronary Syndrome	Additional description: Acute Coronary Syndrome		
subjects affected / exposed	1 / 53 (1.89%)	3 / 55 (5.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
worsening hearing	Additional description: hypoacusis		
subjects affected / exposed	1 / 53 (1.89%)	3 / 55 (5.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Increased inner ear pressure	Additional description: Inner ear disorder		
subjects affected / exposed	1 / 53 (1.89%)	3 / 55 (5.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tinnitus	Additional description: Tinnitus		

subjects affected / exposed	1 / 53 (1.89%)	3 / 55 (5.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ear complete deafness	Additional description: deafness unilateral		
subjects affected / exposed	1 / 53 (1.89%)	3 / 55 (5.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Severe Bladder voiiding disturbance	Additional description: Dysuria		
subjects affected / exposed	1 / 53 (1.89%)	3 / 55 (5.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Active Treatment STR001	Placebo Treatment Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 53 (41.51%)	23 / 55 (41.82%)	
Nervous system disorders			
Balance disorder			
subjects affected / exposed	2 / 53 (3.77%)	4 / 55 (7.27%)	
occurrences (all)	2	4	
Dizziness			
subjects affected / exposed	5 / 53 (9.43%)	5 / 55 (9.09%)	
occurrences (all)	5	6	
Ear and labyrinth disorders			
ear pain			
subjects affected / exposed	4 / 53 (7.55%)	5 / 55 (9.09%)	
occurrences (all)	5	11	
Tinnitus			
subjects affected / exposed	6 / 53 (11.32%)	2 / 55 (3.64%)	
occurrences (all)	7	2	
Vertigo labyrinthine			
subjects affected / exposed	0 / 53 (0.00%)	3 / 55 (5.45%)	
occurrences (all)	0	3	

Gastrointestinal disorders Diarrhea subjects affected / exposed occurrences (all)	 0 / 53 (0.00%) 0	 3 / 55 (5.45%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 October 2015	Amendment 1 - non substantial To clarify inconsistencies in Day numbering throughout the protocol.
19 November 2015	Amendment 2 - non substantial (France only) To clarify vaccination eligibility -vaccination against Streptococcus pneumoniae must be allowed.
24 November 2015	Amendment 3 - non substantial (Germany only) to clarify sample size justification
04 December 2015	Amendment 4 - non substantial (Germany only) to remove text in the protocol not applicable for study population.
26 January 2016	Amendment 5 - non substantial To harmonize the inclusion criterion number 2 with the primary objective.
26 January 2016	Amendment 6 - non-substantial (France only) To clarify vaccination eligibility following the request of the French Health Authorities.
09 February 2016	Amendment 7 - non-substantial (France only) To address a request from the French Health Authorities in order to comply with eligibility criteria of patients for Cochlear Implant surgery in France.
25 February 2016	Amendment 8 - non-substantial the average differences of BCTA and PTA are removed from the protocol as an inclusion criterion as well as in the definition of the efficacy analysis population.
10 June 2016	Amendment 9 - non-substantial include more electrodes/increase age for inclusion criterion/add clarification of use of steroids/adapt number of countries and sites

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported