Clinical trial results:
A two- part, randomized, double-blind, placebo-controlled, parallel-group, efficacy and safety study of SENS-401 in subjects with severe or profound sudden sensorineural hearing loss

Summary

EudraCT number	2018-000812-47
Trial protocol	SK BG CZ GB DE
Global end of trial date	12 January 2022

Results information

Result version number	v1 (current)
This version publication date	30 March 2023
First version publication date	30 March 2023

Trial information

Trial identification

Sponsor protocol code	SENS401-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03603314
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sensorion SA
Sponsor organisation address	375 rue du Professeur Joseph Blayac, Montpellier, France, 34080
Public contact	Serge Fitoussi, SENSORION SA, 0686936412 6 98 37 23 09, contact@sensorion-pharma.com
Scientific contact	Serge Fitoussi, SENSORION SA, 0686936412 6 98 37 23 09, contact@sensorion-pharma.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	04 November 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 November 2021
Global end of trial reached?	Yes
Global end of trial date	12 January 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of SENS-401 on hearing loss in comparison to placebo at the end of the 4-week treatment period.

Protection of trial subjects:

A complete physical examination, blood test and ECG is be performed to make sure patients are not specifically at risk of developing side effects.

Background therapy:

In addition to the study drug administration, the study doctor can prescribe , if not contraindicated, the treatment usually given for SSNHL at the time of teh study, which is an oral corticosteroid.

Evidence for comparator: -

Actual start date of recruitment	15 February 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Slovakia: 12
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Bulgaria: 8
Country: Number of subjects enrolled	Czechia: 9
Country: Number of subjects enrolled	France: 26
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Israel: 31
Country: Number of subjects enrolled	Serbia: 12
Country: Number of subjects enrolled	Turkey: 10
Worldwide total number of subjects	115
EEA total number of subjects	57

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)	98
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Date of First Signed Informed Consent: 15 Feb 2019
Date of Last Subject Contact: 12 Jan 2022
Study Centers: The study was conducted at 32 sites in 10 countries (Bulgaria, Canada, Czech Republic, France, Germany, Israel, Serbia, Slovakia, Turkey, and United Kingdom)

Pre-assignment

Screening details:

Adults with unilateral idiopathic SSNHL or unilateral/bilateral acute acoustic trauma leading to SSNHL.

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

Blinding implementation details:

The SENS-401 and placebo tablet are identical.
Randomisation list has been generated centrally and using a 1:1:1 randomisation ratio was generated for the whole study. The investigator, the sponsor study team, the CRO and subjects was blinded to the IMP administration. The lists of randomisation was stratified by the duration of the disease at baseline (≥24 hours or < 24 hours) and oral corticosteroids intake at baseline (no, yes).

Arms

Are arms mutually exclusive?	Yes
Arm title	29 mg dose group

Arm description:

Patients will receive the study drug (SENS-401) in the form of tablets by mouth, twice a day, during the first 4 weeks after randomization.
SENS-401: 29 mg dose group: 2 tablets of 14.5 mg and 1 tablet of matching placebo, oral route, by mouth, twice a day, during 4 weeks

Arm type	Experimental
Investigational medicinal product name	Arazasetron
Investigational medicinal product code	SENS-401
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

14.5 mg

Arm title	43.5 mg Dose Group

Arm description:

Patients will receive the study drug (SENS-401) in the form of tablets by mouth, twice a day, during the first 4 weeks after randomization.
SENS-401: 43.5 mg dose groupe: 3 tablets of 14.5 mg, oral route, by mouth, twice a day, during 4 weeks

Arm type	Experimental
Investigational medicinal product name	Arazasetron
Investigational medicinal product code	SENS-401
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

14.5 mg

Arm title	Placebo Oral Tablet

Arm description:

Patients will receive the study drug (placebo) in the form of tablets by mouth, twice a day, during the first 4 weeks after randomization.
Placebo Oral Tablet: 3 tablets of matching placebo, oral route, by mouth, twice a day, during 4 weeks

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

Dosage and administration details:

Placebo

Number of subjects in period 1	29 mg dose group	43.5 mg Dose Group	Placebo Oral Tablet
Started	38	39	38
Completed	31	28	35
Not completed	7	11	3
Physician decision	1	1	-
Consent withdrawn by subject	4	5	3
Adverse event, non-fatal	2	-	-
UNKWN	-	1	-
Lost to follow-up	-	3	-
Protocol deviation	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	29 mg dose group
Reporting group description:	
Patients will receive the study drug (SENS-401) in the form of tablets by mouth, twice a day, during the first 4 weeks after randomization. SENS-401: 29 mg dose group: 2 tablets of 14.5 mg and 1 tablet of matching placebo, oral route, by mouth, twice a day, during 4 weeks	
Reporting group title	43.5 mg Dose Group
Reporting group description:	
Patients will receive the study drug (SENS-401) in the form of tablets by mouth, twice a day, during the first 4 weeks after randomization. SENS-401: 43.5 mg dose groupe: 3 tablets of 14.5 mg, oral route, by mouth, twice a day, during 4 weeks	
Reporting group title	Placebo Oral Tablet
Reporting group description:	
Patients will receive the study drug (placebo) in the form of tablets by mouth, twice a day, during the first 4 weeks after randomization. Placebo Oral Tablet: 3 tablets of matching placebo, oral route, by mouth, twice a day, during 4 weeks	

Reporting group values	29 mg dose group	43.5 mg Dose Group	Placebo Oral Tablet
Number of subjects	38	39	38
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)	28	36	34
From 65-84 years	10	3	4
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	54.5	46.9	49.8
standard deviation	± 16.40	± 16.01	± 14.56
Gender categorical Units: Subjects			
Female	14	17	9
Male	24	22	29

Reporting group values	Total		
Number of subjects	115		
Age categorical 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)	98		
From 65-84 years	17		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	40		
Male	75		

End points

End points reporting groups

Reporting group title	29 mg dose group
Reporting group description:	
Patients will receive the study drug (SENS-401) in the form of tablets by mouth, twice a day, during the first 4 weeks after randomization. SENS-401: 29 mg dose group: 2 tablets of 14.5 mg and 1 tablet of matching placebo, oral route, by mouth, twice a day, during 4 weeks	
Reporting group title	43.5 mg Dose Group
Reporting group description:	
Patients will receive the study drug (SENS-401) in the form of tablets by mouth, twice a day, during the first 4 weeks after randomization. SENS-401: 43.5 mg dose groupe: 3 tablets of 14.5 mg, oral route, by mouth, twice a day, during 4 weeks	
Reporting group title	Placebo Oral Tablet
Reporting group description:	
Patients will receive the study drug (placebo) in the form of tablets by mouth, twice a day, during the first 4 weeks after randomization. Placebo Oral Tablet: 3 tablets of matching placebo, oral route, by mouth, twice a day, during 4 weeks	

Primary: Change in Pure Tone Audiometry PTA (dB) (Average of the Hearing Threshold of the 3 Contiguous Most Affected Hearing Frequencies in dB as Identified at Study Entry) From Baseline to the End of Treatment Visit (Day 28 ± 3).

End point title	Change in Pure Tone Audiometry PTA (dB) (Average of the Hearing Threshold of the 3 Contiguous Most Affected Hearing Frequencies in dB as Identified at Study Entry) From Baseline to the End of Treatment Visit (Day 28 ± 3).
End point description:	
Pure Tone Audiometry PTA (dB) thresholds were determined for each ear at 0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz for air conduction and 0.5, 1, 2, 3, 4 kHz for bone conduction. Pure Tone Audiometry PTA (dB) is an hearing test used to identify hearing threshold levels of an individual and enabling determination of the degree hearing loss. A clinically significative improvement is defined as a decrease of at least 10 dB of hearing threshold.	
End point type	Primary
End point timeframe:	
28 days	

End point values	29 mg dose group	43.5 mg Dose Group	Placebo Oral Tablet	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	39	38	
Units: dB				
least squares mean (confidence interval 90%)	-27.754 (-40.534 to -14.974)	-24.931 (-37.793 to -12.069)	-25.214 (-38.310 to -12.119)	

Statistical analyses

Statistical analysis title	P-Value: 29 mg Dose Group vs Placebo

Statistical analysis description:

The null and alternative hypotheses for Part 1 of the study were as follows, where μH, μL and μP were defined as the mean change in PTA of the high dose, low dose, and placebo respectively: H0H: μH - μP = 0, HAH: μH - μP <0 (greater decrease on high dose) H0L: μL - μP = 0, HAL: μL - μP <0 (greater decrease on low dose)

Comparison groups	Placebo Oral Tablet v 29 mg dose group
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3419
Method	Mixed models analysis

Statistical analysis title	P-Value: 43.5 mg Dose Group vs Placebo

Statistical analysis description:

The null and alternative hypotheses for Part 1 of the study were as follows, where μH, μL and μP were defined as the mean change in PTA of the high dose, low dose, and placebo respectively: H0H: μH - μP = 0, HAH: μH - μP <0 (greater decrease on high dose) H0L: μL - μP = 0, HAL: μL - μP <0 (greater decrease on low dose)

Comparison groups	Placebo Oral Tablet v 43.5 mg Dose Group
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5181
Method	Mixed models analysis

Secondary: Change in Pure Tone Audiometry PTA (dB) (Average of the Hearing Threshold of the 2 Most Affected Hearing Frequencies in dB as Identified at Study Entry) From Baseline to the End of Treatment Visit (Day 28 ± 3).

End point title	Change in Pure Tone Audiometry PTA (dB) (Average of the Hearing Threshold of the 2 Most Affected Hearing Frequencies in dB as Identified at Study Entry) From Baseline to the End of Treatment Visit (Day 28 ± 3).

End point description:

Pure Tone Audiometry PTA (dB) thresholds were determined for each ear at 0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz for air conduction and 0.5, 1, 2, 3, 4 kHz for bone conduction.
Pure Tone Audiometry PTA (dB) is an hearing test used to identify hearing threshold levels of an individual and enabling determination of the degree hearing loss.
A clinically significative improvement is defined as a decrease of at least 10 dB of hearing threshold.

End point type	Secondary

End point timeframe:

Day 28

End point values	29 mg dose group	43.5 mg Dose Group	Placebo Oral Tablet	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	39	38	
Units: dB				
least squares mean (confidence interval 90%)	-27.910 (-41.211 to -14.610)	-24.468 (-37.860 to -11.076)	-25.726 (-39.369 to -12.084)	

Statistical analyses

Statistical analysis title	P-Value: 29 mg Dose Group vs Placebo

Statistical analysis description:

The null and alternative hypotheses for Part 1 of the study were as follows, where μH, μL and μP were defined as the mean change in PTA of the high dose, low dose, and placebo respectively: H0H: μH - μP = 0, HAH: μH - μP <0 (greater decrease on high dose) H0L: μL - μP = 0, HAL: μL - μP <0 (greater decrease on low dose)

Comparison groups	29 mg dose group v Placebo Oral Tablet
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3666
Method	Mixed models analysis

Statistical analysis title	P-Value: 43.5 mg Dose Group vs Placebo

Statistical analysis description:

The null and alternative hypotheses for Part 1 of the study were as follows, where μH, μL and μP were defined as the mean change in PTA of the high dose, low dose, and placebo respectively: H0H: μH - μP = 0, HAH: μH - μP <0 (greater decrease on high dose) H0L: μL - μP = 0, HAL: μL - μP <0 (greater decrease on low dose)

Comparison groups	Placebo Oral Tablet v 43.5 mg Dose Group
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5776
Method	Mixed models analysis

Secondary: Change in Pure Tone Audiometry PTA (dB) (the Most Affected Hearing Frequencies in dB as Identified at Study Entry) From Baseline to the End of Treatment Visit (Day 28 ± 3).

End point title	Change in Pure Tone Audiometry PTA (dB) (the Most Affected Hearing Frequencies in dB as Identified at Study Entry) From Baseline to the End of Treatment Visit (Day 28 ± 3).

End point description:

Pure Tone Audiometry PTA (dB) thresholds were determined for each ear at 0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz for air conduction and 0.5, 1, 2, 3, 4 kHz for bone conduction.
Pure Tone Audiometry PTA (dB) is an hearing test used to identify hearing threshold levels of an individual and enabling determination of the degree hearing loss.
A clinically significative improvement is defined as a decrease of at least 10 dB of hearing threshold.

End point type	Secondary

End point timeframe:

Day 28

End point values	29 mg dose group	43.5 mg Dose Group	Placebo Oral Tablet	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	39	38	
Units: dB				
least squares mean (confidence interval 90%)	-30.889 (-44.619 to -17.159)	-30.035 (-43.850 to -16.220)	-29.371 (-43.469 to -15.272)	

Statistical analyses

Statistical analysis title	P-Value: 29 mg Dose Group vs Placebo

Statistical analysis description:

The null and alternative hypotheses for Part 1 of the study were as follows, where μH, μL and μP were defined as the mean change in PTA of the high dose, low dose, and placebo respectively: H0H: μH - μP = 0, HAH: μH - μP <0 (greater decrease on high dose) H0L: μL - μP = 0, HAL: μL - μP <0 (greater decrease on low dose)

Comparison groups	29 mg dose group v Placebo Oral Tablet
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.4094
Method	Mixed models analysis

Statistical analysis title	P-Value: 43.5 mg Dose Group vs Placebo

Statistical analysis description:

The null and alternative hypotheses for Part 1 of the study were as follows, where μH, μL and μP were defined as the mean change in PTA of the high dose, low dose, and placebo respectively: H0H: μH - μP = 0, HAH: μH - μP <0 (greater decrease on high dose) H0L: μL - μP = 0, HAL: μL - μP <0 (greater decrease on low dose)

Comparison groups	Placebo Oral Tablet v 43.5 mg Dose Group
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.4602
Method	Mixed models analysis

Secondary: Change in Pure Tone Audiometry PTA (dB) (Average of the Hearing Threshold of the 3 Most Affected Hearing Frequencies in dB as Identified at Study Entry) From Baseline to the End of Study Visit (Day 84 ± 3).

End point title	Change in Pure Tone Audiometry PTA (dB) (Average of the Hearing Threshold of the 3 Most Affected Hearing Frequencies in dB as Identified at Study Entry) From Baseline to the End of Study Visit (Day 84 ± 3).

End point description:

Pure Tone Audiometry PTA (dB) thresholds were determined for each ear at 0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz for air conduction and 0.5, 1, 2, 3, 4 kHz for bone conduction.
Pure Tone Audiometry PTA (dB) is an hearing test used to identify hearing threshold levels of an individual and enabling determination of the degree hearing loss.
A clinically significative improvement is defined as a decrease of at least 10 dB of hearing threshold.

End point type	Secondary

End point timeframe:

Day 84

End point values	29 mg dose group	43.5 mg Dose Group	Placebo Oral Tablet	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	30	33	
Units: dB				
least squares mean (confidence interval 90%)	-32.469 (-45.229 to -19.708)	-30.070 (-42.881 to -17.259)	-25.399 (-38.363 to -12.435)	

Statistical analyses

Statistical analysis title	P-Value: 29 mg Dose Group vs Placebo

Statistical analysis description:

The null and alternative hypotheses for Part 1 of the study were as follows, where μH, μL and μP were defined as the mean change in PTA of the high dose, low dose, and placebo respectively: H0H: μH - μP = 0, HAH: μH - μP <0 (greater decrease on high dose) H0L: μL - μP = 0, HAL: μL - μP <0 (greater decrease on low dose)

Comparison groups	29 mg dose group v Placebo Oral Tablet
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1269
Method	Mixed models analysis

Statistical analysis title	P-Value: 43.5 mg Dose Group vs Placebo

Statistical analysis description:

The null and alternative hypotheses for Part 1 of the study were as follows, where μH, μL and μP were defined as the mean change in PTA of the high dose, low dose, and placebo respectively: H0H: μH - μP = 0, HAH: μH - μP <0 (greater decrease on high dose) H0L: μL - μP = 0, HAL: μL - μP <0 (greater decrease on low dose)

Comparison groups	Placebo Oral Tablet v 43.5 mg Dose Group

Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2257
Method	Mixed models analysis

Secondary: Change in Speech Discrimination Threshold From Baseline to Day 28

End point title	Change in Speech Discrimination Threshold From Baseline to Day 28

End point description:

The Speech recognition threshold (SRT) (dB) is the minimum hearing level at which an individual can correctly recognize 50% of speech material; the more severe the hearing loss is, the higher SRT is. Spondaic words are the usual and recommended test material for the speech recognition threshold; spondaic words are two-syllable words with equal stress on both syllables (eg, birthday). Per the American Speech-Language-Hearing Association (ASHA) guidelines, subjects were familiarized with the spondaic words prior to the test; they listened to the list of words and indicated if any were unfamiliar. These words could then be eliminated from the list.

End point type	Secondary

End point timeframe:

Day 28

End point values	29 mg dose group	43.5 mg Dose Group	Placebo Oral Tablet	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	39	38	
Units: dB				
least squares mean (confidence interval 90%)	-22.899 (-35.836 to -9.962)	-19.882 (-33.015 to -6.748)	-19.827 (-33.336 to -6.318)	

Statistical analyses

Statistical analysis title	P-Value: 29 mg Dose Group vs Placebo

Statistical analysis description:

The null and alternative hypotheses for Part 1 of the study were as follows, where μH, μL and μP were defined as the mean change in PTA of the high dose, low dose, and placebo respectively: H0H: μH - μP = 0, HAH: μH - μP <0 (greater decrease on high dose) H0L: μL - μP = 0, HAL: μL - μP <0 (greater decrease on low dose)

Comparison groups	29 mg dose group v Placebo Oral Tablet
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3121
Method	Mixed models analysis

Statistical analysis title	P-Value: 43.5 mg Dose Group vs Placebo

Statistical analysis description:

The null and alternative hypotheses for Part 1 of the study were as follows, where μH, μL and μP were defined as the mean change in PTA of the high dose, low dose, and placebo respectively: H0H: μH - μP = 0, HAH: μH - μP <0 (greater decrease on high dose) H0L: μL - μP = 0, HAL: μL - μP <0 (greater decrease on low dose)

Comparison groups	Placebo Oral Tablet v 43.5 mg Dose Group
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4965
Method	Mixed models analysis

Secondary: Change in Speech Discrimination Threshold From Baseline to Day 84

End point title	Change in Speech Discrimination Threshold From Baseline to Day 84

End point description:

The Speech recognition threshold (SRT) (dB) is the minimum hearing level at which an individual can correctly recognize 50% of speech material; the more severe the hearing loss is, the higher SRT is. Spondaic words are the usual and recommended test material for the speech recognition threshold; spondaic words are two-syllable words with equal stress on both syllables (eg, birthday). Per the American Speech-Language-Hearing Association (ASHA) guidelines, subjects were familiarized with the spondaic words prior to the test; they listened to the list of words and indicated if any were unfamiliar. These words could then be eliminated from the list.

End point type	Secondary

End point timeframe:

Day 84

End point values	29 mg dose group	43.5 mg Dose Group	Placebo Oral Tablet	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	30	33	
Units: dB				
least squares mean (confidence interval 90%)	-24.990 (-38.040 to -11.940)	-22.671 (-35.939 to -9.403)	-16.642 (-30.236 to -3.048)	

Statistical analyses

Statistical analysis title	P-Value: 29 mg Dose Group vs Placebo

Statistical analysis description:

The null and alternative hypotheses for Part 1 of the study were as follows, where μH, μL and μP were defined as the mean change in PTA of the high dose, low dose, and placebo respectively: H0H: μH - μP = 0, HAH: μH - μP <0 (greater decrease on high dose) H0L: μL - μP = 0, HAL: μL - μP <0 (greater decrease on low dose)

Comparison groups	29 mg dose group v Placebo Oral Tablet

Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0976
Method	Mixed models analysis

Statistical analysis title	P-Value: 43.5 mg Dose Group vs Placebo

Statistical analysis description:

The null and alternative hypotheses for Part 1 of the study were as follows, where μH, μL and μP were defined as the mean change in PTA of the high dose, low dose, and placebo respectively: H0H: μH - μP = 0, HAH: μH - μP <0 (greater decrease on high dose) H0L: μL - μP = 0, HAL: μL - μP <0 (greater decrease on low dose)

Comparison groups	Placebo Oral Tablet v 43.5 mg Dose Group
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1762
Method	Mixed models analysis

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 84 days	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	29 mg dose group
Reporting group description: Patients will receive the study drug (SENS-401) in the form of tablets by mouth, twice a day, during the first 4 weeks after randomization. SENS-401: 29 mg dose group: tablets of 14.5 mg, oral route, by mouth, twice a day, during 4 weeks	
Reporting group title	43.5 mg Dose Group
Reporting group description: Patients will receive the study drug (SENS-401) in the form of tablets by mouth, twice a day, during the first 4 weeks after randomization. SENS-401: 43.5 mg dose groupe: tablets of 14.5 mg, oral route, by mouth, twice a day, during 4 weeks	
Reporting group title	Placebo Oral Tablet
Reporting group description: Patients will receive the study drug (placebo) in the form of tablets by mouth, twice a day, during the first 4 weeks after randomization. Placebo Oral Tablet: placebo, oral route, by mouth, twice a day, during 4 weeks	

Serious adverse events	29 mg dose group	43.5 mg Dose Group	Placebo Oral Tablet
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 38 (2.63%)	1 / 39 (2.56%)	1 / 38 (2.63%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon neoplasm			
subjects affected / exposed	0 / 38 (0.00%)	1 / 39 (2.56%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 38 (2.63%)	0 / 39 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			

subjects affected / exposed	0 / 38 (0.00%)	0 / 39 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 38 (2.63%)	0 / 39 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	29 mg dose group	43.5 mg Dose Group	Placebo Oral Tablet
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 38 (52.63%)	13 / 39 (33.33%)	4 / 38 (10.53%)
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 38 (10.53%)	0 / 39 (0.00%)	1 / 38 (2.63%)
occurrences (all)	5	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 38 (10.53%)	0 / 39 (0.00%)	0 / 38 (0.00%)
occurrences (all)	6	0	0
Headache			
subjects affected / exposed	6 / 38 (15.79%)	6 / 39 (15.38%)	0 / 38 (0.00%)
occurrences (all)	7	6	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 38 (5.26%)	1 / 39 (2.56%)	2 / 38 (5.26%)
occurrences (all)	2	1	2
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	10 / 38 (26.32%)	6 / 39 (15.38%)	1 / 38 (2.63%)
occurrences (all)	11	7	1
Nausea			
subjects affected / exposed	3 / 38 (7.89%)	2 / 39 (5.13%)	1 / 38 (2.63%)
occurrences (all)	3	2	1

Vomiting			
subjects affected / exposed	2 / 38 (5.26%)	1 / 39 (2.56%)	0 / 38 (0.00%)
occurrences (all)	2	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 38 (5.26%)	0 / 39 (0.00%)	0 / 38 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 38 (5.26%)	0 / 39 (0.00%)	0 / 38 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 38 (0.00%)	2 / 39 (5.13%)	1 / 38 (2.63%)
occurrences (all)	0	2	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 March 2020	Amendment to Inclusion Criteria: -inclusion of bilateral acute acoustic trauma leading to SSNHL - Inclusion of severe hearing loss affecting at least 1 hearing threshold of 50 dB or more amongst the 3 most affected contiguous pure tone frequencies -extension of the window of the onset of symptoms of SHL from 72 hours to 96 hours prior to first study drug intake - Addition of an ancillary study at French military sites - Other updates required by authorities: addition of an exclusion criterion for subjects with significant risks for cardiac arrhythmias, clarification of serotonin syndrome/neuroleptic malignant syndrome AE definitions, as well as harmonisation of the text for the country-specific protocol.
05 February 2021	- Decreased the sample size to 111 for Part 1 - Used a GST with 3 looks planned at 63, 85, and 111 subjects - Change in exclusion criterion 18 regarding formula for renal clearance in subjects over 65

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported