



Clinical trial results:

A multicentre, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of 2 dose regimens of orally administered SENS-111 (100mg and 200mg) given during 4 days in patients suffering from Acute Unilateral Vestibulopathy

Summary

EudraCT number	2016-003927-45
Trial protocol	DE CZ HU ES PL IT
Global end of trial date	15 October 2019

Results information

Result version number	v1 (current)
This version publication date	12 August 2020
First version publication date	12 August 2020
Summary attachment (see zip file)	SENS-111-201 CSR synopsis (SENS111-201 CSR Synopsis 12May20.pdf)

Trial information

Trial identification

Sponsor protocol code	SENS-111-201
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03110458
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sensorion SA
Sponsor organisation address	375 rue du Professeur Joseph Blayac, Montpellier, France, 34080
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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	15 November 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	15 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy of SENS-111 in Acute Unilateral Vestibulopathy (AUV)

Protection of trial subjects:

In exceptional circumstances, when the patient was presenting with a severe, unbearable vertigo lasting more than 4 days, a rescue medication could be given to the patient from Day 5 and onwards.

Background therapy:

No background therapy.

Evidence for comparator:

There is no approved therapy for AUV. Many patients are severely impaired by vertigo, nausea and vomiting in the acute phase: these symptoms are major targets for treatment. Nausea and vomiting are usually treated with antihistamines, mostly dimenhydrinate or even benzodiazepines in severe cases which induce sedation. The effects of corticosteroids and vestibular exercises are still debated. Those treatment were not permitted in the study.

Actual start date of recruitment	16 August 2017
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	Czech Republic: 2
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 31
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Israel: 34
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Korea, Republic of: 29
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	107
EEA total number of subjects	43

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)	92
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The date of first informed consent was 16 August 2017. A total of 134 subjects were screened in 8 countries worldwide and 94 subjects overall out of the 107 subjects in the ITT population completed the study.

Pre-assignment

Screening details:

Out of the 134 participants screened for the trial, 27 were screen failures and were not randomized and 107 participants were randomized onto the trial.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	SENS-111 100mg

Arm description:

1 x 100mg Oral Dispersible Tablet + 1 placebo Oral Dispersible Tablet

Arm type	Experimental
Investigational medicinal product name	SENS-111 100mg
Investigational medicinal product code	SENS-111 100mg
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

SENS-111 100mg is presented as 1 Oral Dispersible Tablet of SENS-111 100mg + 1 Oral Dispersible Tablet of placebo given twice on Day 1, second intake given approximately 12 hours (9 to 15 hours) after the first intake and thereafter given once daily on Days 2 to 5 inclusive. The corresponding total dose will be 500 mg for the entire study.

Administration Route: The tablet should not be swallowed immediately, nor taken with water. The tablet should be kept in the mouth for a few seconds until dispersion is complete.
There is no food restriction.

Arm title	SENS-111 200mg
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Arm description:

2 x 100mg Oral Dispersible Tablets

Arm type	Experimental
Investigational medicinal product name	SENS-111 200 mg
Investigational medicinal product code	SENS-111 200 mg
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

SENS-111 200mg is presented as 2 Oral Dispersible Tablet of SENS-111 100mg given twice on Day 1, second intake given approximately 12 hours (9 to 15 hours) after the first intake and thereafter given once daily on Days 2 to 5 inclusive. The corresponding total dose will be 1000 mg for the entire study.

Administration Route: The tablet should not be swallowed immediately, nor taken with water. The tablet should be kept in the mouth for a few seconds until dispersion is complete.

There is no food restriction.

Arm title	Placebo
Arm description: 2 placebo Oral Dispersible Tablets	
Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	placebo
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo is presented as 2 Oral Dispersible Tablets of placebo given twice on Day 1, second intake given approximately 12 hours (9 to 15 hours) after the first intake and thereafter given once daily on Days 2 to 5 inclusive. The corresponding total dose will be 0 mg for the entire study.

Administration Route: The tablet should not be swallowed immediately, nor taken with water. The tablet should be kept in the mouth for a few seconds until dispersion is complete.
There is no food restriction.

Number of subjects in period 1	SENS-111 100mg	SENS-111 200mg	Placebo
Started	37	36	34
Completed	31	32	31
Not completed	6	4	3
Consent withdrawn by subject	3	1	1
Adverse event, non-fatal	-	1	-
not severe vertigo	-	-	1
other	2	2	1
Protocol deviation	1	-	-

Baseline characteristics

Reporting groups

Reporting group title	SENS-111 100mg
Reporting group description: 1 x 100mg Oral Dispersible Tablet + 1 placebo Oral Dispersible Tablet	
Reporting group title	SENS-111 200mg
Reporting group description: 2 x 100mg Oral Dispersible Tablets	
Reporting group title	Placebo
Reporting group description: 2 placebo Oral Dispersible Tablets	

Reporting group values	SENS-111 100mg	SENS-111 200mg	Placebo
Number of subjects	37	36	34
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	49.4 ± 12.89	51.6 ± 14.14	51.1 ± 12.82
Gender categorical Units: Subjects			
Female	14	8	11
Male	23	28	23
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	20	21	19
Not Reported	16	15	15
Unknown	1	0	0
Body Weight Units: kilogram(s) arithmetic mean standard deviation	82.2 ± 22.10	81.6 ± 18.9	80.1 ± 16.37

Reporting group values	Total		
Number of subjects	107		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	-		
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Gender categorical			
Units: Subjects			
Female	33		
Male	74		
Ethnicity			
Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	60		
Not Reported	46		
Unknown	1		
Body Weight			
Units: kilogram(s)			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	SENS-111 100mg
Reporting group description: 1 x 100mg Oral Dispersible Tablet + 1 placebo Oral Dispersible Tablet	
Reporting group title	SENS-111 200mg
Reporting group description: 2 x 100mg Oral Dispersible Tablets	
Reporting group title	Placebo
Reporting group description: 2 placebo Oral Dispersible Tablets	

Primary: Standing vertigo intensity

End point title	Standing vertigo intensity
End point description: The primary efficacy endpoint was the Area Under Curve (AUC) for the vertigo intensity measured by the Vertigo Intensity Visual Analogue Scale (VI-VAS) in standing position over the 4 treatment days (8 post-baseline assessments). The vertigo Intensity VAS is a non-anchored 10cm horizontal line. Patients were asked to rate the intensity of their vertigo making a vertical mark crossing the horizontal 10 cm line to indicate the severity from 0-100 when 0 indicates no severity and 100 indicates worse severity	
End point type	Primary
End point timeframe: during 4 days of treatment	

End point values	SENS-111 100mg	SENS-111 200mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	35	31	
Units: Vertigo Intensity Visual Analogue Scale				
arithmetic mean (standard error)	165.10 (\pm 71.02)	155.10 (\pm 83.06)	136.60 (\pm 62.61)	

Statistical analyses

Statistical analysis title	SENS-111 100mg versus placebo
Comparison groups	SENS-111 100mg v Placebo

Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8466
Method	ANCOVA

Statistical analysis title	SENS-111 pooled versus placebo
Comparison groups	SENS-111 100mg v SENS-111 200mg v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8411
Method	ANCOVA

Statistical analysis title	SENS-111 200mg versus placebo
Comparison groups	SENS-111 200mg v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7677
Method	ANCOVA

Secondary: Worst spontaneous vertigo intensity

End point title	Worst spontaneous vertigo intensity
End point description:	
Worst spontaneous vertigo intensity measured by the AUC of the worst Vertigo Intensity Visual Analogue Scale (VI-VAS) over the 4 treatment days (8 post-baseline assessments). The vertigo Intensity VAS is a non-anchored 10cm horizontal line. Patients were asked to rate the intensity of their vertigo making a vertical mark crossing the horizontal 10 cm line to indicate the severity from 0-100 when 0 indicates no severity and 100 indicates worse severity	
End point type	Secondary
End point timeframe:	
over the 4 treatment days (Day 5)	

End point values	SENS-111 100mg	SENS-111 200mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	32	27	
Units: Vertigo Intensity Visual Analogue Scale				
arithmetic mean (standard deviation)	180.1 (± 67.20)	170.4 (± 89.83)	140.8 (± 64.66)	

Statistical analyses

Statistical analysis title	SENS-111 pooled versus placebo
Comparison groups	SENS-111 100mg v SENS-111 200mg v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9538
Method	ANCOVA

Secondary: Proprioception D28 (Change from Baseline of the total score of the Romberg test)

End point title	Proprioception D28 (Change from Baseline of the total score of the Romberg test)
End point description: Change from Baseline of the total score of the six conditions of the Romberg test (in this test higher values are indicating a higher ability to stand unassisted, total minimum: 0 maximum: 6) at the end of treatment (EOT) (Day 5) and at the end of study (EOS) (Day 28)	
End point type	Secondary
End point timeframe: End of treatment (Day 5) to End of study (Day 28).	

End point values	SENS-111 100mg	SENS-111 200mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	33	26	
Units: absolute value Romberg test				
arithmetic mean (standard deviation)	2.70 (± 1.60)	3.00 (± 1.64)	3.20 (± 1.46)	

Statistical analyses

Statistical analysis title	SENS-111 pooled versus placebo
Comparison groups	SENS-111 100mg v SENS-111 200mg v Placebo

Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.393
Method	ANCOVA

Secondary: Vestibular spontaneous nystagmus D28

End point title	Vestibular spontaneous nystagmus D28
End point description: Change from Baseline of the Peak Slow Phase Velocity of the Peripheral Vestibular Spontaneous Nystagmus, measured by Oculography in Darkness at End of treatment (Day 5) and End of Study (Day 28)	
End point type	Secondary
End point timeframe: 28 days compared to baseline	

End point values	SENS-111 100mg	SENS-111 200mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	25	23	
Units: degrees per second				
arithmetic mean (standard deviation)	-4.80 (± 15.10)	-7.9 (± 12.76)	-7.7 (± 11.59)	

Statistical analyses

No statistical analyses for this end point

Secondary: Nausea severity

End point title	Nausea severity
End point description: Nausea Severity measured by the Area under the Curve of the Nausea Intensity Visual Analogue Scale (NI-VAS) over the 4 Treatment Days (8 Post-baseline Assessments). Patients were asked to rate the intensity of their nausea making a vertical mark crossing the 10 cm line to indicate the severity from 0-100 when 0 indicates no severity and 100 indicates worse severity.	
End point type	Secondary
End point timeframe: over the 4 Treatment Days (Day 5)	

End point values	SENS-111 100mg	SENS-111 200mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	35	31	
Units: Nausea Intensity Visual Analogue Scale				
arithmetic mean (standard deviation)	93.00 (± 78.39)	91.50 (± 79.73)	92.60 (± 57.28)	

Statistical analyses

Statistical analysis title	SENS-111 pooled versus placebo
Comparison groups	SENS-111 100mg v SENS-111 200mg v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5324
Method	ANCOVA

Secondary: Proprioception D5 (Change from Baseline of the total score of the Romberg test)

End point title	Proprioception D5 (Change from Baseline of the total score of the Romberg test)
End point description:	Change from Baseline of the total score of the six conditions of the Romberg test (in this test higher values are indicating a higher ability to stand unassisted, total minimum: 0 maximum: 6) at the end of treatment (EOT) (Day 5) and at the end of study (EOS) (Day 28)
End point type	Secondary
End point timeframe:	After 4 days of treatment (D5)

End point values	SENS-111 100mg	SENS-111 200mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	32	26	
Units: absolute value Romberg test				
arithmetic mean (standard deviation)	2.10 (± 1.46)	2.00 (± 1.79)	2.40 (± 1.45)	

Statistical analyses

Statistical analysis title	SENS-111 pooled versus placebo
Comparison groups	SENS-111 100mg v SENS-111 200mg v Placebo

Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3166
Method	ANCOVA

Secondary: Vestibular spontaneous nystagmus D5

End point title	Vestibular spontaneous nystagmus D5
End point description: Change from Baseline of the Peak Slow Phase Velocity of the Peripheral Vestibular Spontaneous Nystagmus, measured by Oculography in Darkness at End of treatment (Day 5) and end of study (EOS) (Day 28)	
End point type	Secondary
End point timeframe: after 4 days of treatment (D5)	

End point values	SENS-111 100mg	SENS-111 200mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	27	25	
Units: degrees per second				
arithmetic mean (standard deviation)	-2.80 (± 10.86)	-3.0 (± 6.72)	-3.50 (± 5.32)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

28 days

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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Reporting groups

Reporting group title	SENS-111 100mg
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Reporting group description:

Treatment emergent adverse events are displayed.

A total of 9 subjects were affected by non serious adverse events. With the frequency threshold of 5%, 4 subjects reported non-serious adverse events.

Reporting group title	Placebo
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Reporting group description:

Treatment emergent adverse events are displayed

A total of 12 subjects were affected by non serious adverse events. With the frequency threshold of 5%, 7 subjects reported non-serious adverse events.

Reporting group title	SENS-111 200mg
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Reporting group description:

Treatment emergent adverse events are displayed

A total of 14 subjects were affected by non serious adverse events. With the frequency threshold of 5%, 5 subjects reported non-serious adverse events.

Serious adverse events	SENS-111 100mg	Placebo	SENS-111 200mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 36 (0.00%)	0 / 32 (0.00%)	1 / 36 (2.78%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Diverticular perforation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 32 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	SENS-111 100mg	Placebo	SENS-111 200mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 36 (11.11%)	7 / 32 (21.88%)	5 / 36 (13.89%)

Injury, poisoning and procedural complications Extra dose administered subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	2 / 32 (6.25%) 2	0 / 36 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 3	7 / 32 (21.88%) 8	4 / 36 (11.11%) 6
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 32 (0.00%) 0	2 / 36 (5.56%) 2
Metabolism and nutrition disorders Folate deficiency subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	0 / 32 (0.00%) 0	0 / 36 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 February 2017	<p>This amendment was prepared to address Grounds for Non-acceptance raised during the Voluntary Harmonisation Procedure and included the following changes:</p> <ul style="list-style-type: none">- Exclusion criterion no. 28 was amended to exclude subjects (male or female) who were unwilling to use 1 of the highly effective contraception therapies listed in the exclusion criteria. In addition, an appendix was added to the protocol to provide complete guidance on highly effective birth control. Also the wording "effective contraception" was changed to "highly effective contraception" throughout the protocol.- Inclusion criterion no. 1 was amended to include an upper age limit and to provide a justification for the selected upper age limit. The sponsor proposed an upper age limit of 75 years as being most representative of the target subject population.- a new section Unblinding Procedure was added to the protocol. A complete discussion of unblinding procedures using the Interactive Web Response System was presented in this new section- protocol's withdrawal criteria was modified to include the worsening of nausea or vertigo as demonstrated on 2 successive VAS scale scores. Additionally, the criteria were expanded to include the onset of new neurological symptoms and hearing loss.- some statement were added indicating that:<ul style="list-style-type: none">*biological samples were to be analyzed locally and destroyed after the analyses. No further uses of the samples were planned for additional research.* no change or amendment to the protocol would be implemented before approval was received by the regulatory authority and ethics committees.* no protocol waivers were to be accepted and any protocol deviation will be assessed by the sponsor. In the event of breach of fundamental obligations including but not limited to breach of the clinical trial protocol, breach of the applicable laws and regulations or breach of the ICH guideline on GCP, the sponsor will report major noncompliance to the Regulatory Authorities
08 September 2017	<ul style="list-style-type: none">• Exclusion criterion no. 22 on contraception was amendment to indicate that contraception had to be used for at least 3 months after the last IMP intake• at some specific sites, an ancillary test using the Caloric test or vHIT were conducted• clarification that consent and screening were to be done no more than 12 hours apart
05 November 2018	<ul style="list-style-type: none">- clarification that around 38 sites in Europe, Israel, USA, and South Korea were planned to be involved in the study- update of sample size calculation so that the number of randomized subjects was reduced to 105 (35 subjects per treatment arm)- Exclusion criterion no. 16 updated so to exclude subjects if they had taken more than 3 doses of the listed concomitant medications- The ECG assessment was moved from V2 to V1 (Screening) and Romberg tests were added at V2, V3, and V4- "Unrelated" was added as an assessment option of AE relationship

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported