



Clinical trial results:

A randomized, cross-over, placebo controlled, and meclizine calibrated study to assess the safety and pharmacodynamic effects of SENS-111 (100 mg and 200 mg) single dose in healthy subjects exposed to experimental motion

Summary

EudraCT number	2018-000777-80
Trial protocol	NL
Global end of trial date	23 November 2018

Results information

Result version number	v1 (current)
This version publication date	18 April 2022
First version publication date	18 April 2022

Trial information

Trial identification

Sponsor protocol code	SENS111-202
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	Judith LAREDO, Sensorion SA, +33 434087116, judith.laredo@sensorion-pharma.com
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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	22 July 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 November 2018
Global end of trial reached?	Yes
Global end of trial date	23 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Objective:

- To confirm the absence of sedative effects and therefore the maintenance of vigilance with SENS-111 in subjects exposed to a vestibular conflict

Protection of trial subjects:

The subjects will be exposed to a rotatory movement while sitting in a chair. This is expected to induce mild to moderate nausea/vomiting and other motion associated symptoms. Patient very susceptible to motion sickness will be excluded from the study. Participants will be instructed that the goal of the experiment is not to make them feel too uncomfortable. If at any time they feel their comfort level prevented them from continuing, they should inform the experimenter and the rotation will be stopped immediately.

Additionally, the operator will monitor the participant's responses on the scale for levels of sickness. If the participants report any "severe" symptoms, the operator will stop the rotation. The test will be terminated as soon as the participant indicates he cannot continue, takes action to physically remove the dark mask, or does not respond to verbal questions.

Subjects will be under constant surveillance during the trial days. They will return home by taxi after the investigator has checked the subject symptoms, and will be advised to call the study site in case of persistent effects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 August 2018
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	Netherlands: 34
Worldwide total number of subjects	34
EEA total number of subjects	34

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)	34
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were included at TNO Soesterberg, the Netherlands between August 14, 2018 (first enrollment date) and November 23, 2018 (last subject completed date).

Pre-assignment

Screening details:

Healthy subjects, non-smokers, and susceptible to motion sickness were recruited for the study.

41 subjects were screened, 7 screen failures occurred. 5 of the 34 subjects enrolled were dropped out, of which 2 were replaced.

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

Blinding implementation details:

In this cross-over design all subjects received all treatments, the order of which was based on a randomization table. The SENS-111 ODT and placebo ODT were identical. The meclizine capsule and placebo capsule were also identical. The investigator, the sponsor study team, the CRO or subjects were blinded to the Investigational drug administration. The randomization code was broken at the trial's end and after all data was entered into the database, after database lock, the results were analyzed.

Arms

Are arms mutually exclusive?	No
Arm title	SENS-111 100mg

Arm description:

First dose regimen : SENS-111 100 mg: One (1) SENS-111 ODT, one (1) placebo ODT and four (4) placebo meclizine capsules

Subjects received the 4 dose regimens; each dose regimen per trial-day with a 7-day wash-out duration between trial-days, in a randomized order.

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

Dosage and administration details:

ODTs were placed in the mouth without water. Dissolution was expected in less than 10 seconds.

Investigational medicinal product name	Placebo Meclizine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Buccal use

Dosage and administration details:

Capsules were administered orally with about 240 mL of water at ambient temperature.

Investigational medicinal product name	Placebo SENS 111
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Dispersible tablet
Routes of administration	Buccal use

Dosage and administration details:

ODTs were placed in the mouth without water. Dissolution was expected in less than 10 seconds.

Arm title	SENS-111 200 mg
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Arm description:

Second dose regimen : SENS-111 200 mg: Two (2) SENS-111 ODT, and four (4) placebo meclizine capsules

Subjects received the 4 dose regimens; each dose regimen per trial-day with a 7-day wash-out duration between trial-days, in a randomized order.

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

Dosage and administration details:

ODTs were placed in the mouth without water. Dissolution was expected in less than 10 seconds.

Investigational medicinal product name	Placebo Meclizine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Buccal use

Dosage and administration details:

Capsules were administered orally with about 240 mL of water at ambient temperature.

Arm title	Meclizine 50 mg
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Arm description:

Third dose regimen : Meclizine 50 mg: Two (2) placebo ODTs and four (4) meclizine encapsulated tablets

Subjects received the 4 dose regimens; each dose regimen per trial-day with a 7-day wash-out duration between trial-days, in a randomized order.

Arm type	Active comparator
Investigational medicinal product name	Meclizine 50 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Buccal use

Dosage and administration details:

Capsules were administered orally with about 240 mL of water at ambient temperature.

Investigational medicinal product name	Placebo SENS 111
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet
Routes of administration	Buccal use

Dosage and administration details:

ODTs were placed in the mouth without water. Dissolution was expected in less than 10 seconds.

Arm title	Placebo condition
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Arm description:

Fourth dose regimen : Placebo condition: Two (2) placebo ODTs and four (4) placebo meclizine capsules

Subjects received the 4 dose regimens; each dose regimen per trial-day with a 7-day wash-out duration between trial-days, in a randomized order.

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

Dosage and administration details:

Capsules were administered orally with about 240 mL of water at ambient temperature.

Investigational medicinal product name	Placebo SENS 111
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet
Routes of administration	Buccal use

Dosage and administration details:

ODTs were placed in the mouth without water. Dissolution was expected in less than 10 seconds.

Number of subjects in period 1	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg
Started	32	31	31
Completed	29	31	30
Not completed	3	0	1
Consent withdrawn by subject	3	-	1

Number of subjects in period 1	Placebo condition
Started	31
Completed	30
Not completed	1
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
Reporting group description:	
31 out of 34 subjects were included in both the sedation and efficacy analysis, with 30 subjects exposed to medizine, 30 subjects exposed to placebo, 29 subjects exposed to SENS-111 100mg and 31 subjects exposed to SENS-111 200mg.	

Reporting group values	Overall trial	Total	
Number of subjects	34	34	
Age categorical			
34 males who were randomized: age between 18 and 45 years, average age 27.9 years. 31 males who are included in the analysis: age between 18 and 45 years, average age 27.9 years . 29 males who completed all four test days: age between 18 and 45 years, average age 28.0 years.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	34	34	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Subjects included were all males.			
Units: Subjects			
Female	0	0	
Male	34	34	

End points

End points reporting groups

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

First dose regimen : SENS-111 100 mg: One (1) SENS-111 ODT, one (1) placebo ODT and four (4) placebo meclizine capsules

Subjects received the 4 dose regimens; each dose regimen per trial-day with a 7-day wash-out duration between trial-days, in a randomized order.

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

Second dose regimen : SENS-111 200 mg: Two (2) SENS-111 ODT, and four (4) placebo meclizine capsules

Subjects received the 4 dose regimens; each dose regimen per trial-day with a 7-day wash-out duration between trial-days, in a randomized order.

Reporting group title	Meclizine 50 mg
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Reporting group description:

Third dose regimen : Meclizine 50 mg: Two (2) placebo ODTs and four (4) meclizine encapsulated tablets

Subjects received the 4 dose regimens; each dose regimen per trial-day with a 7-day wash-out duration between trial-days, in a randomized order.

Reporting group title	Placebo condition
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Reporting group description:

Fourth dose regimen : Placebo condition: Two (2) placebo ODTs and four (4) placebo meclizine capsules

Subjects received the 4 dose regimens; each dose regimen per trial-day with a 7-day wash-out duration between trial-days, in a randomized order.

Primary: Sedation assessed by Pepsy test battery - Choice reaction time - Reaction Time

End point title	Sedation assessed by Pepsy test battery - Choice reaction time - Reaction Time
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End point description:

Choice reaction time (CRT): This test evaluates the speed at which a subject is able to respond to a complex visual stimulus. The complex stimuli consist of the words "YES" or "NO", which appear randomly at the center of a computer screen. The subject is instructed to press the green button of the keyboard as quickly as possible when the word YES appears on the screen, or to press the red button as quickly as possible when the word NO appears on the screen. Fifty targets (25 "YES" and 25 "NO") are presented to the subject. Performance will be assessed as the speed of processing (in ms), and the answer accuracy expressed as the percentage of correct answers. The total duration of the test is about 3mn.

End point type	Primary
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End point timeframe:

At the visit 2, visit 3, visit 4 and visit 5. Each visit are separated to an other visit with a wash-out period of 7 days (-/+ days).

The test was done at predose, and after dose at 1h30, 2h30, 4h00 and 5h00.

End point values	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg	Placebo condition
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	30	30
Units: mSec				
arithmetic mean (standard deviation)				
Mean RT (mSec) in change from baseline at 1h30	21.0 (± 73.2)	32.8 (± 75.3)	59.3 (± 121.9)	52.8 (± 130.3)
Mean RT (mSec) in change from baseline at 2h30	63.3 (± 104.9)	48.6 (± 76.1)	92.6 (± 117.7)	49.8 (± 73.6)
Mean RT (mSec) in change from baseline at 4h00	52.2 (± 122.5)	51.7 (± 86.8)	109.8 (± 141.1)	72.6 (± 128.8)
Mean RT (mSec) in change from baseline at 5h00	52.1 (± 130.8)	53.6 (± 88.8)	128.1 (± 150.3)	62.2 (± 96.7)

Statistical analyses

Statistical analysis title	P-Value : Placebo vs SENS-111 100 mg
Statistical analysis description:	
Comparisons of Treatments on Changes from Baseline	
P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.	
Comparison groups	SENS-111 100mg v Placebo condition
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.841
Method	Adjusted Dunnett test

Statistical analysis title	P-Value : Placebo vs SENS-111 200 mg
Statistical analysis description:	
Comparisons of Treatments on Changes from Baseline	
P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.	
Comparison groups	Placebo condition v SENS-111 200 mg
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8472
Method	Adjusted Dunnett test

Statistical analysis title	P-Value : Placebo vs Meclizine 50 mg
Statistical analysis description:	
Comparisons of Treatments on Changes from Baseline	
P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.	
Comparison groups	Placebo condition v Meclizine 50 mg

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1128
Method	Adjusted Dunnett test

Primary: Sedation assessed by Pepsy Test Battery - Choice reaction time - Accuracy

End point title	Sedation assessed by Pepsy Test Battery - Choice reaction time - Accuracy
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End point description:

Choice reaction time (CRT): This test evaluates the speed at which a subject is able to respond to a complex visual stimulus. The complex stimuli consist of the words "YES" or "NO", which appear randomly at the center of a computer screen. The subject is instructed to press the green button of the keyboard as quickly as possible when the word YES appears on the screen, or to press the red button as quickly as possible when the word NO appears on the screen. Fifty targets (25 "YES" and 25 "NO") are presented to the subject. Performance will be assessed as the speed of processing (in ms), and the answer accuracy expressed as the percentage of correct answers. The total duration of the test is about 3mn.

End point type	Primary
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End point timeframe:

At the visit 2, visit 3, visit 4 and visit 5. Each visit are separated to an other visit with a wash-out period of 7 days (-/+ days).

The test was done at predose, and after dose at 1h30, 2h30, 4h00 and 5h00.

End point values	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg	Placebo condition
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	30	30
Units: % Correct responses				
arithmetic mean (standard deviation)				
% Correct responses in change to baseline at 1h30	1.1 (± 3.6)	0.3 (± 3.1)	0.4 (± 3.6)	0.8 (± 2.9)
% Correct responses in change to baseline at 2h30	1.0 (± 4.7)	0.8 (± 3.2)	0.2 (± 4.1)	2.0 (± 4.3)
% Correct responses in change to baseline at 4h00	0.6 (± 4.0)	0.5 (± 2.7)	-0.3 (± 4.2)	1.0 (± 3.9)
% Correct responses in change to baseline at 5h00	0.0 (± 3.9)	0.2 (± 3.3)	-1.0 (± 3.4)	0.3 (± 3.6)

Statistical analyses

Statistical analysis title	P-Value : Placebo vs SENS-111 100 mg
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Statistical analysis description:

Comparisons of Treatments on Changes from Baseline

P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.

Comparison groups	SENS-111 100mg v Placebo condition
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Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9311
Method	Adjusted Dunnett test

Statistical analysis title	P-Value : Placebo vs SENS-111 200 mg
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Statistical analysis description:

Comparisons of Treatments on Changes from Baseline

P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.

Comparison groups	Placebo condition v SENS-111 200 mg
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7452
Method	Adjusted Dunnett test

Statistical analysis title	P-Value : Placebo vs Meclizine 50 mg
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Statistical analysis description:

Comparisons of Treatments on Changes from Baseline

P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.

Comparison groups	Placebo condition v Meclizine 50 mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2454
Method	Adjusted Dunnett test

Primary: Sedation assessed by Pepsy test battery - Choice reaction time - Number of errors

End point title	Sedation assessed by Pepsy test battery - Choice reaction time - Number of errors ^[1]
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End point description:

Choice reaction time (CRT): This test evaluates the speed at which a subject is able to respond to a complex visual stimulus. The complex stimuli consist of the words "YES" or "NO", which appear randomly at the center of a computer screen. The subject is instructed to press the green button of the keyboard as quickly as possible when the word YES appears on the screen, or to press the red button as quickly as possible when the word NO appears on the screen. Fifty targets (25 "YES" and 25 "NO") are presented to the subject. Performance will be assessed as the speed of processing (in ms), and the answer accuracy expressed as the percentage of correct answers. The total duration of the test is about 3mn.

End point type	Primary
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End point timeframe:

At the visit 2, visit 3, visit 4 and visit 5. Each visit are separated to an other visit with a wash-out period of 7 days (-/+ days).

The test was done at predose, and after dose at 1h30, 2h30, 4h00 and 5h00.

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: No statistical analyses have been specified for this end point.

End point values	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg	Placebo condition
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	30	30
Units: Numbers of errors				
arithmetic mean (standard deviation)				
Mean Errors in change from baseline at 1h30	-0.5 (± 1.8)	-0.1 (± 1.6)	-0.3 (± 1.7)	-0.4 (± 1.5)
Mean Errors in change from baseline at 2h30	-0.7 (± 1.9)	-0.5 (± 1.6)	-0.2 (± 2.2)	-1.0 (± 2.1)
Mean Errors in change from baseline at 4h00	-0.3 (± 2.0)	-0.3 (± 1.3)	0.0 (± 2.0)	-0.5 (± 2.0)
Mean Errors in change from baseline at 5h00	-0.0 (± 1.9)	-0.1 (± 1.6)	0.1 (± 1.5)	-0.2 (± 1.7)

Statistical analyses

No statistical analyses for this end point

Primary: Sedation assessed by Pepsy test battery - Choice reaction time - Number of false alarms

End point title	Sedation assessed by Pepsy test battery - Choice reaction time - Number of false alarms ^[2]
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End point description:

Choice reaction time (CRT): This test evaluates the speed at which a subject is able to respond to a complex visual stimulus. The complex stimuli consist of the words "YES" or "NO", which appear randomly at the center of a computer screen. The subject is instructed to press the green button of the keyboard as quickly as possible when the word YES appears on the screen, or to press the red button as quickly as possible when the word NO appears on the screen. Fifty targets (25 "YES" and 25 "NO") are presented to the subject. Performance will be assessed as the speed of processing (in ms), and the answer accuracy expressed as the percentage of correct answers. The total duration of the test is about 3mn.

End point type	Primary
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End point timeframe:

At the visit 2, visit 3, visit 4 and visit 5. Each visit are separated to an other visit with a wash-out period of 7 days (-/+ days).

The test was done at predose, and after dose at 1h30, 2h30, 4h00 and 5h00.

Notes:

[2] - 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: No statistical analyses have been specified for this end point.

End point values	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg	Placebo condition
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	30	30
Units: Number of false alarms				
arithmetic mean (standard deviation)				
Mean False alarms in change from baseline at 1h30	-0.2 (± 1.2)	-0.4 (± 1.3)	0.2 (± 1.0)	-0.2 (± 0.9)
Mean False alarms in change from baseline at 2h30	0.0 (± 1.2)	-0.3 (± 1.1)	0.5 (± 1.3)	-0.1 (± 1.5)
Mean False alarms in change from baseline at 4h00	-0.1 (± 1.9)	-0.3 (± 1.0)	0.3 (± 1.3)	0.0 (± 2.0)
Mean False alarms in change from baseline at 5h00	-0.1 (± 1.6)	-0.2 (± 1.3)	0.3 (± 1.0)	0.3 (± 1.5)

Statistical analyses

No statistical analyses for this end point

Primary: Sedation assessed by Pepsy test battery - Numeric Working Memory (NWM) - Reaction time

End point title	Sedation assessed by Pepsy test battery - Numeric Working Memory (NWM) - Reaction time
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End point description:

A series of 5 digits is presented to the subject to hold in memory. This is followed by a series of 30 probe digits for each of which the subject has to decide whether or not, it is in the original series and to press the "YES" or "NO" response button on the keyboard as appropriate, as quickly as possible. This test is performed 3 times with series of different digits. This test lasts approximately 2 minutes.

End point type	Primary
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End point timeframe:

At the visit 2, visit 3, visit 4 and visit 5. Each visit are separated to an other visit with a wash-out period of 7 days (-/+ days).

The test was done at predose, and after dose at 1h30, 2h30, 4h00 and 5h00.

End point values	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg	Placebo condition
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	30	30
Units: mSec				
arithmetic mean (standard deviation)				
Mean RT (mSec) in change from baseline at 1h30	20.3 (± 125.5)	40.7 (± 150.7)	83.3 (± 157.1)	17.0 (± 138.2)
Mean RT (mSec) in change from baseline at 2h30	55.4 (± 203.0)	4.3 (± 137.6)	119.0 (± 226.7)	46.5 (± 159.7)
Mean RT (mSec) in change from baseline at 4h00	31.0 (± 148.5)	-10.2 (± 104.0)	126.5 (± 188.0)	63.4 (± 156.0)
Mean RT (mSec) in change from baseline at 5h00	59.3 (± 182.4)	-37.3 (± 147.3)	121.8 (± 197.3)	49.3 (± 206.0)

Statistical analyses

Statistical analysis title	P-Value : Placebo vs SENS-111 100 mg
Statistical analysis description: Comparisons of Treatments on Changes from Baseline	
P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.	
Comparison groups	SENS-111 100mg v Placebo condition
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9995
Method	Adjusted Dunnett test

Statistical analysis title	P-Value : Placebo vs SENS-111 200 mg
Statistical analysis description: Comparisons of Treatments on Changes from Baseline	
P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.	
Comparison groups	Placebo condition v SENS-111 200 mg
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3347
Method	Adjusted Dunnett test

Statistical analysis title	P-Value : Placebo vs Meclizine 50 mg
Statistical analysis description: Comparisons of Treatments on Changes from Baseline	
P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.	
Comparison groups	Placebo condition v Meclizine 50 mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.065
Method	Adjusted Dunnett test

Primary: Sedation assessed by Pepsy test battery - Numeric Working Memory

(NWM) - Accuracy

End point title	Sedation assessed by Pepsy test battery - Numeric Working Memory (NWM) - Accuracy
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End point description:

A series of 5 digits is presented to the subject to hold in memory. This is followed by a series of 30 probe digits for each of which the subject has to decide whether or not, it is in the original series and to press the "YES" or "NO" response button on the keyboard as appropriate, as quickly as possible. This test is performed 3 times with series of different digits. This test lasts approximately 2 minutes.

End point type	Primary
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End point timeframe:

At the visit 2, visit 3, visit 4 and visit 5. Each visit are separated to an other visit with a wash-out period of 7 days (-/+ days).

The test was done at predose, and after dose at 1h30, 2h30, 4h00 and 5h00

End point values	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg	Placebo condition
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	30	30
Units: % Correct responses				
arithmetic mean (standard deviation)				
% Correct responses in change to baseline at 1h30	-0.5 (± 3.7)	-0.7 (± 7.4)	-1.0 (± 5.1)	-0.8 (± 5.2)
% Correct responses in change to baseline at 2h30	-1.6 (± 4.4)	0.3 (± 6.8)	-3.6 (± 8.6)	-1.6 (± 6.6)
% Correct responses in change to baseline at 4h00	-2.6 (± 3.7)	-0.2 (± 5.1)	-3.0 (± 7.2)	-3.6 (± 8.8)
% Correct responses in change to baseline at 5h00	-2.1 (± 5.2)	-0.8 (± 4.6)	-4.4 (± 8.8)	-1.9 (± 6.2)

Statistical analyses

Statistical analysis title	P-Value : Placebo vs SENS-111 100 mg
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Statistical analysis description:

Comparisons of Treatments on Changes from Baseline

P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.

Comparison groups	SENS-111 100mg v Placebo condition
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9936
Method	Adjusted Dunnett test

Statistical analysis title	P-Value : Placebo vs SENS-111 200 mg
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Statistical analysis description:

Comparisons of Treatments on Changes from Baseline

P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.

Comparison groups	Placebo condition v SENS-111 200 mg
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Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3488
Method	Adjusted Dunnett test

Statistical analysis title	P-Value : Placebo vs Meclizine 50 mg
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Statistical analysis description:

Comparisons of Treatments on Changes from Baseline

P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.

Comparison groups	Placebo condition v Meclizine 50 mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6754
Method	Adjusted Dunnett test

Primary: Sedation assessed by Pepsy test battery - Numeric Working Memory (NWM) - Missed digits

End point title	Sedation assessed by Pepsy test battery - Numeric Working Memory (NWM) - Missed digits ^[3]
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End point description:

A series of 5 digits is presented to the subject to hold in memory. This is followed by a series of 30 probe digits for each of which the subject has to decide whether or not, it is in the original series and to press the "YES" or "NO" response button on the keyboard as appropriate, as quickly as possible. This test is performed 3 times with series of different digits. This test lasts approximately 2 minutes.

End point type	Primary
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End point timeframe:

At the visit 2, visit 3, visit 4 and visit 5. Each visit are separated to an other visit with a wash-out period of 7 days (-/+ days).

The test was done at predose, and after dose at 1h30, 2h30, 4h00 and 5h00.

Notes:

[3] - 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: No statistical analyses have been specified for this end point.

End point values	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg	Placebo condition
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	30	30
Units: Number of missed digits				
arithmetic mean (standard deviation)				
Mean missed digits in change from baseline at 1h30	-0.0 (± 0.2)	0.0 (± 0.4)	0.1 (± 0.3)	0.0 (± 0.3)
Mean missed digits in change from baseline at 2h30	-0.0 (± 0.2)	-0.0 (± 0.3)	0.3 (± 0.9)	0.0 (± 0.3)
Mean missed digits in change from baseline at 3h00	0.1 (± 0.4)	-0.0 (± 0.3)	0.1 (± 0.6)	0.1 (± 0.3)
Mean missed digits in change from baseline at 5h00	0.0 (± 0.3)	0.0 (± 0.5)	0.4 (± 1.3)	0.1 (± 0.4)

Statistical analyses

No statistical analyses for this end point

Primary: Sedation assessed by Pepsy test battery - Numeric Working Memory (NWM) - Number of false alarms

End point title	Sedation assessed by Pepsy test battery - Numeric Working Memory (NWM) - Number of false alarms ^[4]
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End point description:

A series of 5 digits is presented to the subject to hold in memory. This is followed by a series of 30 probe digits for each of which the subject has to decide whether or not, it is in the original series and to press the "YES" or "NO" response button on the keyboard as appropriate, as quickly as possible. This test is performed 3 times with series of different digits. This test lasts approximately 2 minutes.

End point type	Primary
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End point timeframe:

At the visit 2, visit 3, visit 4 and visit 5. Each visit are separated to an other visit with a wash-out period of 7 days (-/+ days).

The test was done at predose, and after dose at 1h30, 2h30, 4h00 and 5h00

Notes:

[4] - 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: No statistical analyses have been specified for this end point.

End point values	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg	Placebo condition
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	30	30
Units: Number of false alarms				
arithmetic mean (standard deviation)				
Mean False alarms in change from baseline at 1h30	0.2 (± 1.1)	0.2 (± 2.2)	0.2 (± 1.5)	0.2 (± 1.6)
Mean False alarms in change from baseline at 2h30	0.5 (± 1.3)	-0.1 (± 2.0)	0.8 (± 2.0)	0.4 (± 1.9)
Mean False alarms in change from baseline at 4h00	0.7 (± 1.1)	0.1 (± 1.6)	0.8 (± 2.1)	1.0 (± 2.5)
Mean False alarms in change from baseline at 5h00	0.6 (± 1.4)	0.2 (± 1.4)	0.9 (± 2.0)	0.5 (± 1.8)

Statistical analyses

No statistical analyses for this end point

Primary: Sedation assessed by Pepsy Test Battery - Spatial Working Memory - Mean reaction time

End point title	Sedation assessed by Pepsy Test Battery - Spatial Working Memory - Mean reaction time
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End point description:

A picture of a house is presented on the screen with 4 of its 9 windows lit. The subject has to memorize the position of the lit windows. For each of the 36 subsequent presentations of the house, the subject has to decide whether or not the window actually lit was also lit in the original presentation. The subject respond by pressing the "YES" or "NO" buttons as appropriate, as quickly as possible. This test lasts approximately 2 to 3 minutes.

End point type	Primary
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End point timeframe:

At the visit 2, visit 3, visit 4 and visit 5. Each visit are separated to an other visit with a wash-out period of 7 days (-/+ days).

The test was done at predose, and after dose at 1h30, 2h30, 4h00 and 5h00.

End point values	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg	Placebo condition
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	30	30
Units: mSec				
arithmetic mean (standard deviation)				
Mean RT (mSec) in change from baseline at 1h30	15.9 (± 182.4)	0.1 (± 124.8)	-7.5 (± 263.3)	-22.4 (± 176.5)
Mean RT (mSec) in change from baseline at 2h30	34.0 (± 207.9)	-12.8 (± 118.1)	-30.3 (± 331.3)	15.1 (± 121.4)
Mean RT (mSec) in change from baseline at 4h00	50.7 (± 312.9)	38.7 (± 236.5)	48.0 (± 386.0)	18.0 (± 177.4)
Mean RT (mSec) in change from baseline at 5h00	24.9 (± 198.9)	-5.7 (± 115.6)	-5.4 (± 312.9)	-64.2 (± 175.6)

Statistical analyses

Statistical analysis title	P-Value : Placebo vs SENS-111 100 mg
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Statistical analysis description:

Comparisons of Treatments on Changes from Baseline

P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.

Comparison groups	SENS-111 100mg v Placebo condition
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Number of subjects included in analysis	59
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Analysis specification	Pre-specified
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Analysis type	superiority
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P-value	= 0.6821
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Method	Adjusted Dunnett test
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Statistical analysis title	P-Value : Placebo vs SENS-111 200 mg
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Statistical analysis description:

Comparisons of Treatments on Changes from Baseline

P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.

Comparison groups	SENS-111 200 mg v Placebo condition
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Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9634
Method	Adjusted Dunnett test

Statistical analysis title	P-Value : Placebo vs Meclizine 50 mg
Statistical analysis description:	
Comparisons of Treatments on Changes from Baseline	
P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.	
Comparison groups	Placebo condition v Meclizine 50 mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9818
Method	Adjusted Dunnett test

Primary: Sedation assessed by Pepsy Test Battery - Spatial Working Memory - Accuracy

End point title	Sedation assessed by Pepsy Test Battery - Spatial Working Memory - Accuracy
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End point description:

A picture of a house is presented on the screen with 4 of its 9 windows lit. The subject has to memorize the position of the lit windows. For each of the 36 subsequent presentations of the house, the subject has to decide whether or not the window actually lit was also lit in the original presentation. The subject respond by pressing the "YES" or "NO" buttons as appropriate, as quickly as possible. This test lasts approximately 2 to 3 minutes.

End point type	Primary
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End point timeframe:

At the visit 2, visit 3, visit 4 and visit 5. Each visit are separated to an other visit with a wash-out period of 7 days (-/+ days).

The test was done at predose, and after dose at 1h30, 2h30, 4h00 and 5h00.

End point values	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg	Placebo condition
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	30	30
Units: % Correct responses				
arithmetic mean (standard deviation)				
% Correct responses in change to baseline at 1h30	-3.0 (± 10.6)	1.0 (± 3.5)	-0.7 (± 7.7)	-0.6 (± 3.7)
% Correct responses in change to baseline at 2h30	-1.2 (± 11.1)	-0.4 (± 6.6)	0.0 (± 10.0)	-4.6 (± 12.0)
% Correct responses in change to baseline at 4h00	-2.3 (± 10.4)	-3.6 (± 13.0)	-1.6 (± 10.9)	-3.8 (± 11.1)
% Correct responses in change to baseline at 5h00	-2.7 (± 9.1)	-1.3 (± 4.7)	-2.2 (± 10.9)	-2.7 (± 9.0)

Statistical analyses

Statistical analysis title	P-Value : Placebo vs SENS-111 100 mg
Statistical analysis description: Comparisons of Treatments on Changes from Baseline	
P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.	
Comparison groups	SENS-111 100mg v Placebo condition
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.92
Method	Adjusted Dunnett test

Statistical analysis title	P-Value : Placebo vs SENS-111 200 mg
Statistical analysis description: Comparisons of Treatments on Changes from Baseline	
P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.	
Comparison groups	Placebo condition v SENS-111 200 mg
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.2689
Method	Adjusted Dunnett test

Statistical analysis title	P-Value : Placebo vs Meclizine 50 mg
Statistical analysis description: Comparisons of Treatments on Changes from Baseline	
P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.	
Comparison groups	Placebo condition v Meclizine 50 mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.308
Method	Adjusted Dunnett test

Primary: Sedation assessed by Pepsy Test Battery - Rapid Visual Information

Processing - Reaction Time

End point title	Sedation assessed by Pepsy Test Battery - Rapid Visual Information Processing - Reaction Time
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End point description:

The Rapid Visual Information Processing (RVIP) is a serial detection task devised by Bakan, aiming to evaluate sustained attention and working memory. RVIP has been used extensively in psychopharmacological studies of the cholinergic system. The RVP displays a series of 1000 digits at a rate of 100 digits every 70 seconds as stimuli. Digits appear in the center of a computer screen. The subject is instructed to press the space bar of the keyboard as quickly as possible when he/she detects a sequence of 3 consecutive odds or 3 consecutive even digits. On average, 80 sequences (40 odd and 40 event sequences) are presented over 10 minutes. A minimum of 5 digits and a maximum of 30 digits are separating 2 consecutive sequences. The subject is given 1500 msec to respond (correct response, accuracy) after the presentation of the third digit of each sequence. Responses obtained at any other time are counted as errors.

End point type	Primary
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End point timeframe:

At the visit 2, visit 3, visit 4 and visit 5. Each visit are separated to an other visit with a wash-out period of 7 days (-/+ days).

The test was done at predose, and after dose at 1h30, 2h30, 4h00 and 5h00.

End point values	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg	Placebo condition
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	30	30
Units: mSec				
arithmetic mean (standard deviation)				
Mean RT (mSec) in change from baseline at 1h30	-5.0 (± 57.7)	16.7 (± 53.9)	-0.1 (± 46.6)	0.6 (± 62.9)
Mean RT (mSec) in change from baseline at 2h30	12.6 (± 68.8)	5.6 (± 52.4)	39.7 (± 62.9)	13.6 (± 48.5)
Mean RT (mSec) in change from baseline at 4h00	-15.7 (± 66.4)	0.4 (± 67.2)	46.5 (± 65.4)	3.4 (± 66.1)
Mean RT (mSec) in change from baseline at 5h00	-13.3 (± 49.4)	6.7 (± 63.8)	42.0 (± 67.2)	-11.4 (± 58.0)

Statistical analyses

Statistical analysis title	P-Value : Placebo vs SENS-111 100 mg
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Statistical analysis description:

Comparisons of Treatments on Changes from Baseline

P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.

Comparison groups	SENS-111 100mg v Placebo condition
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8793
Method	Adjusted Dunnett test

Statistical analysis title	P-Value : Placebo vs SENS-111 200 mg
Statistical analysis description:	
Comparisons of Treatments on Changes from Baseline	
P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.	
Comparison groups	Placebo condition v SENS-111 200 mg
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9233
Method	Adjusted Dunnett test

Statistical analysis title	P-Value : Placebo vs Meclizine 50 mg
Statistical analysis description:	
Comparisons of Treatments on Changes from Baseline	
P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.	
Comparison groups	Placebo condition v Meclizine 50 mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0316
Method	Adjusted Dunnett test

Primary: Sedation assessed by Pepsy Test Battery - Rapid Visual Information Processing - Accuracy

End point title	Sedation assessed by Pepsy Test Battery - Rapid Visual Information Processing - Accuracy
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End point description:

The Rapid Visual Information Processing (RVIP) is a serial detection task devised by Bakan, aiming to evaluate sustained attention and working memory. RVIP has been used extensively in psychopharmacological studies of the cholinergic system. The RVP displays a series of 1000 digits at a rate of 100 digits every 70 seconds as stimuli. Digits appear in the center of a computer screen. The subject is instructed to press the space bar of the keyboard as quickly as possible when he/she detects a sequence of 3 consecutive odds or 3 consecutive even digits. On average, 80 sequences (40 odd and 40 event sequences) are presented over 10 minutes. A minimum of 5 digits and a maximum of 30 digits are separating 2 consecutive sequences. The subject is given 1500 msec to respond (correct response, accuracy) after the presentation of the third digit of each sequence. Responses obtained at any other time are counted as errors.

End point type	Primary
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End point timeframe:

At the visit 2, visit 3, visit 4 and visit 5. Each visit are separated to an other visit with a wash-out period of 7 days (-/+ days).

The test was done at predose, and after dose at 1h30, 2h30, 4h00 and 5h00.

End point values	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg	Placebo condition
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	30	30
Units: % Correct responses				
arithmetic mean (standard deviation)				
% Correct responses in change to baseline at 1h30	-3.4 (± 12.7)	-4.3 (± 12.5)	-5.0 (± 14.1)	-1.7 (± 13.0)
% Correct responses in change to baseline at 2h30	-5.9 (± 12.8)	-4.2 (± 12.1)	-6.7 (± 12.6)	-2.7 (± 13.1)
% Correct responses in change to baseline at 4h00	-5.2 (± 13.2)	-3.0 (± 11.1)	-9.8 (± 13.9)	-2.9 (± 10.8)
% Correct responses in change to baseline at 5h00	-6.2 (± 12.9)	-3.2 (± 14.2)	-10.0 (± 16.2)	-2.0 (± 12.9)

Statistical analyses

Statistical analysis title	P-Value : Placebo vs SENS-111 100 mg
Statistical analysis description: Comparisons of Treatments on Changes from Baseline P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.	
Comparison groups	SENS-111 100mg v Placebo condition
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3964
Method	Adjusted Dunnett test

Statistical analysis title	Placebo vs SENS-111 200 mg
Statistical analysis description: Comparisons of Treatments on Changes from Baseline P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.	
Comparison groups	Placebo condition v SENS-111 200 mg
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8911
Method	Adjusted Dunnett test

Statistical analysis title	Placebo vs Meclizine 50 mg
Statistical analysis description: Comparisons of Treatments on Changes from Baseline P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.	
Comparison groups	Placebo condition v Meclizine 50 mg

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0344
Method	Adjusted Dunnett test

Primary: Sedation assessed by Pepsy Test Battery - Rapid Visual Information Processing - Number of missed digits

End point title	Sedation assessed by Pepsy Test Battery - Rapid Visual Information Processing - Number of missed digits
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End point description:

The Rapid Visual Information Processing (RVIP) is a serial detection task devised by Bakan, aiming to evaluate sustained attention and working memory. RVIP has been used extensively in psychopharmacological studies of the cholinergic system. The RVP displays a series of 1000 digits at a rate of 100 digits every 70 seconds as stimuli. Digits appear in the center of a computer screen. The subject is instructed to press the space bar of the keyboard as quickly as possible when he/she detects a sequence of 3 consecutive odds or 3 consecutive even digits. On average, 80 sequences (40 odd and 40 event sequences) are presented over 10 minutes. A minimum of 5 digits and a maximum of 30 digits are separating 2 consecutive sequences. The subject is given 1500 msec to respond (correct response, accuracy) after the presentation of the third digit of each sequence. Responses obtained at any other time are counted as errors.

End point type	Primary
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End point timeframe:

At the visit 2, visit 3, visit 4 and visit 5. Each visit are separated to an other visit with a wash-out period of 7 days (-/+ days).

The test was done at predose, and after dose at 1h30, 2h30, 4h00 and 5h00.

End point values	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg	Placebo condition
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	30	30
Units: Number of missed digits				
arithmetic mean (standard deviation)				
Mean missed digits in change from baseline at 1h30	2.8 (± 7.6)	2.2 (± 8.2)	4.1 (± 8.1)	4.1 (± 12.8)
Mean missed digits in change from baseline at 2h30	6.4 (± 9.2)	4.8 (± 6.4)	8.1 (± 6.7)	5.1 (± 8.9)
Mean missed digits in change from baseline at 4h00	8.2 (± 11.2)	7.0 (± 11.4)	12.6 (± 11.2)	9.2 (± 9.1)
Mean missed digits in change from baseline at 5h00	7.4 (± 9.8)	6.6 (± 12.1)	10.6 (± 10.2)	8.1 (± 9.8)

Statistical analyses

Statistical analysis title	P-Value : Placebo vs SENS-111 100 mg
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Statistical analysis description:

Comparisons of Treatments on Changes from Baseline

P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.

Comparison groups	SENS-111 100mg v Placebo condition
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Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9981
Method	Adjusted Dunnett test

Statistical analysis title	P-Value : Placebo vs SENS-111 200 mg
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Statistical analysis description:

Comparisons of Treatments on Changes from Baseline

P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.

Comparison groups	Placebo condition v SENS-111 200 mg
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6896
Method	Adjusted Dunnett test

Statistical analysis title	P-Value : Placebo vs Meclizine 50 mg
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Statistical analysis description:

Comparisons of Treatments on Changes from Baseline

P-value estimated using the adjusted Dunnett test to compare an active treatment to placebo.

Comparison groups	Placebo condition v Meclizine 50 mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3753
Method	Adjusted Dunnett test

Primary: Sedation assessed by Pepsy Test Battery - Rapid Visual Information Processing - Number of false alarms

End point title	Sedation assessed by Pepsy Test Battery - Rapid Visual Information Processing - Number of false alarms ^[5]
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End point description:

The Rapid Visual Information Processing (RVIP) is a serial detection task devised by Bakan, aiming to evaluate sustained attention and working memory. RVIP has been used extensively in psychopharmacological studies of the cholinergic system. The RVP displays a series of 1000 digits at a rate of 100 digits every 70 seconds as stimuli. Digits appear in the center of a computer screen. The subject is instructed to press the space bar of the keyboard as quickly as possible when he/she detects a sequence of 3 consecutive odds or 3 consecutive even digits. On average, 80 sequences (40 odd and 40 event sequences) are presented over 10 minutes. A minimum of 5 digits and a maximum of 30 digits are separating 2 consecutive sequences. The subject is given 1500 msec to respond (correct response, accuracy) after the presentation of the third digit of each sequence. Responses obtained at any other time are counted as errors.

End point type	Primary
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End point timeframe:

At the visit 2, visit 3, visit 4 and visit 5. Each visit are separated to an other visit with a wash-out period of 7 days (-/+ days).

The test was done at predose, and after dose at 1h30, 2h30, 4h00 and 5h00.

Notes:

[5] - 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: No statistical analyses have been specified for this end point.

End point values	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg	Placebo condition
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	30	30
Units: Number of false alarms				
arithmetic mean (standard deviation)				
Mean False alarms in change from baseline at 1h30	1.8 (± 7.9)	2.0 (± 5.8)	2.5 (± 6.8)	0.7 (± 5.4)
Mean False alarms in change from baseline at 2h30	2.2 (± 6.8)	1.6 (± 6.9)	2.3 (± 6.5)	2.4 (± 8.6)
Mean False alarms in change from baseline at 4h00	2.0 (± 8.3)	1.0 (± 6.2)	4.2 (± 7.6)	1.2 (± 6.2)
Mean False alarms in change from baseline at 5h00	2.5 (± 8.3)	0.1 (± 7.6)	4.0 (± 7.7)	1.6 (± 9.5)

Statistical analyses

No statistical analyses for this end point

Primary: Sedation assessed by VigTrack - Mean Tracking Error

End point title	Sedation assessed by VigTrack - Mean Tracking Error ^[6]
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End point description:

The task will be performed on a computer screen. During the tracking task, subjects have to steer a blue dot using a joystick, so that it is kept below a red dot in the center of the display. The blue dot is programmed to move continuously from the center of the display.

While tracking, subjects have to perform the vigilance task. Inside the red dot, a black square alternates with a diamond, once per second. Sometimes, a hexagon is presented.

The duration of this test will be 10 minutes and performance measures include:

- root mean square tracking error
- percentage omissions
- number of false reactions
- reaction times

End point type	Primary
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End point timeframe:

At the visit 2, visit 3, visit 4 and visit 5. Each visit are separated to an other visit with a wash-out period of 7 days (-/+ days).

The test was done at predose, and after dose at 1h30, 2h30, 4h00 and 5h00.

Notes:

[6] - 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: No statistical analyses have been specified for this end point.

End point values	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg	Placebo condition
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	30	29
Units: Number of tracking error				
arithmetic mean (standard deviation)				
Mean Tracking error in change to baseline at 1h30	1.0 (± 28.2)	-2.3 (± 8.4)	3.6 (± 14.8)	-2.0 (± 12.1)
Mean Tracking error in change to baseline at 2h30	2.1 (± 30.2)	2.3 (± 23.9)	12.0 (± 19.4)	-4.8 (± 15.6)
Mean Tracking error in change to baseline at 4h00	1.8 (± 17.1)	2.1 (± 18.1)	22.0 (± 26.2)	0.8 (± 22.4)
Mean Tracking error in change to baseline at 5h00	1.5 (± 28.9)	-1.7 (± 20.6)	17.7 (± 40.2)	2.8 (± 23.3)

Statistical analyses

No statistical analyses for this end point

Primary: Sedation assessed by VigTrack - Percentage omissions

End point title	Sedation assessed by VigTrack - Percentage omissions ^[7]
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End point description:

The task will be performed on a computer screen. During the tracking task, subjects have to steer a blue dot using a joystick, so that it is kept below a red dot in the center of the display. The blue dot is programmed to move continuously from the center of the display.

While tracking, subjects have to perform the vigilance task. Inside the red dot, a black square alternates with a diamond, once per second. Sometimes, a hexagon is presented.

The duration of this test will be 10 minutes and performance measures include:

- root mean square tracking error
- percentage omissions
- number of false reactions
- reaction times

End point type	Primary
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End point timeframe:

At the visit 2, visit 3, visit 4 and visit 5. Each visit are separated to an other visit with a wash-out period of 7 days (-/+ days).

The test was done at predose, and after dose at 1h30, 2h45, 4h00 and 5h15.

Notes:

[7] - 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: No statistical analyses have been specified for this end point.

End point values	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg	Placebo condition
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	30	29
Units: Percentage omissions				
arithmetic mean (standard deviation)				
Mean % omissions in change from baseline - 1h30	2.2 (± 8.6)	1.7 (± 5.1)	4.6 (± 8.6)	1.4 (± 4.3)
Mean % omissions in change from baseline - 2h45	4.1 (± 10.8)	2.9 (± 5.2)	7.5 (± 8.7)	2.5 (± 5.0)
Mean % omissions in change from baseline - 4h00	4.6 (± 8.0)	5.0 (± 7.9)	13.0 (± 15.0)	6.7 (± 7.8)

Mean % omissions in change from baseline - 5h15	5.8 (± 12.4)	4.8 (± 6.7)	12.8 (± 13.4)	6.2 (± 8.6)
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Statistical analyses

No statistical analyses for this end point

Primary: Sedation assessed by VigTrack - Mean Reaction time

End point title	Sedation assessed by VigTrack - Mean Reaction time ^[8]
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End point description:

The task will be performed on a computer screen. During the tracking task, subjects have to steer a blue dot using a joystick, so that it is kept below a red dot in the center of the display. The blue dot is programmed to move continuously from the center of the display.

While tracking, subjects have to perform the vigilance task. Inside the red dot, a black square alternates with a diamond, once per second. Sometimes, a hexagon is presented.

The duration of this test will be 10 minutes and performance measures include:

- root mean square tracking error
- percentage omissions
- number of false reactions
- reaction times

End point type	Primary
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End point timeframe:

At the visit 2, visit 3, visit 4 and visit 5. Each visit are separated to an other visit with a wash-out period of 7 days (-/+ days).

The test was done at predose, and after dose at 1h30, 2h45, 4h00 and 5h15.

Notes:

[8] - 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: No statistical analyses have been specified for this end point.

End point values	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg	Placebo condition
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	30	29
Units: mSec				
arithmetic mean (standard deviation)				
Mean RT (mSec) in change from baseline at 1h30	0.02 (± 0.04)	0.03 (± 0.05)	0.05 (± 0.06)	0.04 (± 0.04)
Mean RT (mSec) in change from baseline at 2h45	0.06 (± 0.05)	0.05 (± 0.05)	0.08 (± 0.04)	0.07 (± 0.04)
Mean RT (mSec) in change from baseline at 4h00	0.06 (± 0.06)	0.07 (± 0.06)	0.11 (± 0.05)	0.08 (± 0.06)
Mean RT (mSec) in change from baseline at 5h15	0.07 (± 0.06)	0.06 (± 0.05)	0.11 (± 0.05)	0.08 (± 0.04)

Statistical analyses

No statistical analyses for this end point

Primary: Sedation assessed by VigTrack - Number of False reactions

End point title	Sedation assessed by VigTrack - Number of False reactions ^[9]
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End point description:

The task will be performed on a computer screen. During the tracking task, subjects have to steer a blue dot using a joystick, so that it is kept below a red dot in the center of the display. The blue dot is programmed to move continuously from the center of the display.

While tracking, subjects have to perform the vigilance task. Inside the red dot, a black square alternates with a diamond, once per second. Sometimes, a hexagon is presented.

The duration of this test will be 10 minutes and performance measures include:

- root mean square tracking error
- percentage omissions
- number of false reactions
- reaction times

End point type	Primary
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End point timeframe:

At the visit 2, visit 3, visit 4 and visit 5. Each visit are separated to an other visit with a wash-out period of 7 days (-/+ days).

The test was done at predose, and after dose at 1h30, 2h45, 4h00 and 5h15.

Notes:

[9] - 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: No statistical analyses have been specified for this end point.

End point values	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg	Placebo condition
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	30	29
Units: Number of False reactions				
arithmetic mean (standard deviation)				
Mean False reaction in change from baseline - 1h30	0.03 (± 1.3)	-0.1 (± 1.3)	-0.5 (± 1.4)	-0.3 (± 1.6)
Mean False reaction in change from baseline - 2h45	0.1 (± 0.8)	0.1 (± 1.7)	0.0 (± 1.9)	0.0 (± 1.6)
Mean False reaction in change from baseline - 4h00	0.0 (± 1.3)	0.1 (± 2.1)	0.8 (± 2.1)	0.7 (± 1.9)
Mean False reaction in change from baseline - 5h15	0.1 (± 1.6)	0.7 (± 2.1)	0.4 (± 3.2)	0.2 (± 1.7)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Any AE occurring after the subject has signed the informed consent until the end of the study participation and within 30 days following the last treatment day must be fully recorded on the subject's eCRF.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

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

First dose regimen : SENS-111 100 mg: One (1) SENS-111 ODT, one (1) placebo ODT and four (4) placebo meclizine capsules

Subjects received the 4 dose regimens; each dose regimen per trial-day with a 7-day wash-out duration between trial-days, in a randomized order.

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

Second dose regimen : SENS-111 200 mg: Two (2) SENS-111 ODT, and four (4) placebo meclizine capsules

Subjects received the 4 dose regimens; each dose regimen per trial-day with a 7-day wash-out duration between trial-days, in a randomized order.

Reporting group title	Meclizine 50 mg
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Reporting group description:

Third dose regimen : Meclizine 50 mg: Two (2) placebo ODTs and four (4) meclizine encapsulated tablets

Subjects received the 4 dose regimens; each dose regimen per trial-day with a 7-day wash-out duration between trial-days, in a randomized order.

Reporting group title	Placebo condition
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Reporting group description:

Fourth dose regimen : Placebo condition: Two (2) placebo ODTs and four (4) placebo meclizine capsules

Subjects received the 4 dose regimens; each dose regimen per trial-day with a 7-day wash-out duration between trial-days, in a randomized order.

Serious adverse events	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 33 (0.00%)	0 / 30 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Placebo condition		
Total subjects affected by serious adverse events			

subjects affected / exposed	0 / 30 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	SENS-111 100mg	SENS-111 200 mg	Meclizine 50 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 30 (3.33%)	1 / 33 (3.03%)	2 / 30 (6.67%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 30 (0.00%)	0 / 33 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Epigastric discomfort			
subjects affected / exposed	1 / 30 (3.33%)	0 / 33 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Flu			
subjects affected / exposed	0 / 30 (0.00%)	1 / 33 (3.03%)	1 / 30 (3.33%)
occurrences (all)	0	1	1

Non-serious adverse events	Placebo condition		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Epigastric discomfort			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Flu			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported