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

Published: 23-05-2018
Last updated: 12-04-2024

The Primary objective is to confirm the maintenance of vigilance with SENS-111.Secondary objectives are:* to confirm the maintenance of working memory, and cognitive function; * to confirm the pharmacodynamics effect of SENS-111 on symptoms...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON46445

Source
ToetsingOnline

Brief title
SENS-111

Condition

- Other condition

Synonym
Nauseau & vigiliance

Health condition

bij gezonde proefpersonen; mate van misselijkheid en behoud van alertheid na inname medicatie

Research involving

Human

Sponsors and support

Primary sponsor: Sensorion
Source(s) of monetary or material Support: Sensorion

Intervention

Keyword: Experimental motion, Meclizine, SENS-111, Vgilance

Outcome measures

Primary outcome

The primary endpoints reflecting sedation will be assessed by the change of

performance over time, compared to baseline, including all test parameters of

the

* Vigilance & Tracking test

* Pepsy psychomotor test battery;

Secondary outcome

The main secondary endpoints reflecting sedation will be assessed by the change

over time, compared to baseline, of

* Subjective alertness measured by the Stanford Sleepiness Scale.

The main secondary endpoint reflecting efficacy will be assessed by

* The severity of nausea and associated symptoms assessed by the MISC during

the rotary chair run and by the change over time, compared to baseline.

* The change over time, compared to baseline, of balance performance as

measured by the Balance Test.

Other study end-point

Includes the change versus baseline in the diameter of the pupil measured by static pupillometry test and the following safety endpoints:

* Overall tolerability: incidence, severity and nature of adverse events and SAE throughout the study course

* Clinical chemistry and hematology parameters

In order to send subject home safely, different medical checks will be done during intake and end of trial day (follow finger movement with eyes, Romberg test, Hand-eye coordination test and misery). Also a short 5 minutes psychomotor vigilance task (PVT) will be conducted. See document K End of trial day medical check.pdf.

Study description

Background summary

Sensorion is developing SENS-111, a H4 antagonist, 100mg and 200mg as a treatment of acute unilateral vertigo (AUV), a rare vestibular disorder. Based on preclinical and clinical studies, SENS-111 was confirmed to modulate the peripheral vestibular apparatus; to reduce symptoms (such as vertigo and nystagmus) associated with vestibular dysfunction; and to be safe and well tolerated. The proposed study is aiming at confirming that SENS-111 (at the potential therapeutic doses) is devoid of anticholinergic properties in an experimental situation of an example of a sensory conflict between parts of the vestibular system, and can therefore be used safely in this population.
Based on the underlying mechanism of action, preclinical safety and clinical safety studies, it is expected/assumed that SENS-111 will maintain cognitive performance and avoid sedation. While other antihistaminines (such as Meclizine as an antihistamine H1) causes major sides effects including sedation, and cognitive disturbances.

Study objective

The Primary objective is to confirm the maintenance of vigilance with SENS-111.
Secondary objectives are:
* to confirm the maintenance of working memory, and cognitive function;
* to confirm the pharmacodynamics effect of SENS-111 on symptoms experimentally induced by motion
* assess the safety of SENS-111

Study design

The study is a 4-period, 4-treatment (SENS-111 100mg, SENS-111 200mg, placebo and meclizine) double-blind, double dummy, cross over design with a randomized sequence order.

Intervention

Subjects will receive the following treatment once, one week apart, in a random order
SENS-111 100mg: 1 ODT100mg SENS-111 and 1 ODT placebo and 4 placebo meclizine oral capsules
SENS-111 200mg: 2 ODT 100mg SENS-111 and 4 placebo meclizine oral capsules
Placebo: 2 ODT placebo and 4 placebo meclizine oral capsules
Meclizine 50mg: 2 ODT Placebo and and 4 meclizine 12,5mg oral encapsulated tablets
During the trial days, they will be exposed to a rotatory movement, while sitting in a chair for induction of nausea.

Study burden and risks

The study will include a total of 6 visits: a screening visit, 4 experimental visits when the subjects will receive the study drug and will be exposed to an experimental rotation (rotating chair), and a follow up visit by phone call to confirm the safety of the patient. The tests will be conducted one week apart. Subjects will be requested to fill in questionnaires and scales, and tests on a screen during the inclusion visit and during the experimental visits to assess the severity of symptoms induced by motion, cognition and vigilance. Usual laboratory tests will be performed at entry and at the end of the study.
SENS-111 has been given to more than 170 subjects, healthy or with allergic rhinitis or with AUV, at 500mg single dose or up to 250mg for 7 days. SENS-111 was well tolerated and only mild to moderate adverse events were reported. The most frequent adverse events reported both in SENS-111 and placebo were nausea, vomiting, somnolence, abdominal pain, abnormal faeces, diarrhoea and headache.
Meclizine has been widely used and is sold as an over the counter medication for the treatment of vertigo and nausea/ vomiting induced by motion. Risks associated with the intake of the drug are well known and includes hypersensitivity to the drug and adverse effects related to the anticholinergic properties. Subjects will be warned of the possibility of drowsiness and

cautioned against driving a car or operating dangerous machinery. Also, alcoholic beverages are to be avoided while taking this drug. Subjects with asthma, glaucoma, or enlargement of the prostate gland will be excluded from the study due to the risk of worsening. Anaphylactoid reactions, drowsiness, dry mouth, headache, fatigue, vomiting and, on rare occasions, blurred vision have been reported.
The subjects will be exposed to a rotatory movement sitting in a chair. This is expected to induce mild to moderate nausea/vomiting and other motion associated symptoms. Patient will be constantly followed, and monitored to avoid dramatic effects.
No individual benefit is expected from participating in this study for a given subject. It is expected that conducting the study in a homogeneous population, in standardized condition, using a calibrator will provide reliable evaluation of the effect of SENS-111 on vigilance, and potential activity in a model of sensory conflict.

Contacts

Public
Sensorion

Rue du Professeur Joseph Blayac 375
Montpellier 34080
FR
Scientific
Sensorion

Rue du Professeur Joseph Blayac 375
Montpellier 34080
FR

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Male
2. Aged *18 years and * 45 years
3. Susceptible to motion sickness defined as MSSQ*short within 10th to 95th percentiles
4. Signed and dated written informed consent.

Exclusion criteria

1. History of acute or chronic vestibular disorder, tinnitus or hearing loss, or inner ear problem
2. Past history of seizures or convulsions
3. Past history of migraine or hyperemesis
4. Subjects with known allergy to meclizine, or to any other histamine antagonist
5. Known severe adverse drug reaction e.g. clinical symptoms of cardiac rhythm disturbances
6. Subjects with known asthma
7. History of alcohol or drug abuse
8. Current smoker
9. Current participation in another clinical trial
10. Treatment with any investigational agent within 4 weeks prior to randomization or 5 half-lives of the investigational drug (whichever is longer)
11. Subject with known narrow angle glaucoma,
12. Subject with known prostate enlargement or history of urine retention
13. Subject with infection or inflammatory process during screening or at inclusion
14. Positive urine screening for drugs
15. Any abnormality on 12-lead electrocardiogram (ECG), in particular QTc prolongation defined by: QTc >470 ms
16. Clinically significant abnormal blood pressure (>140/90 mmHg) or significant abnormal heart rate (arrhythmia, or tachycardia or bradycardia).
17. Known history of, or concomitant hepatic, gastrointestinal, cardiovascular, respiratory, neurological, psychiatric, hematological, renal, or dermatological disease, or any condition, psychiatric, substance abuse, or otherwise, that, in the opinion of the Investigator might interfere with the evaluation of study treatment or warrant exclusion.
18. Abnormal laboratory findings:
a. Creatininemia >1.5 upper limit of normal (ULN))
b. ALAT and/or ASAT > 1.5 x ULN
c. Hemoglobin 10 g/ml and/or
d. Neutrophils <1500/ml and/or
e. Platelets <100 000 /ml
19. Subject is unavailable to complete the study (including all follow-up visits) and comply with study restrictions.
20. Subjects who, in the opinion of the Investigator, have significant medical or psychosocial

findings that warrant exclusion. Examples of significant problems include, but are not limited to other serious non-malignancy-associated medical conditions that may be expected to limit life expectancy or significantly increase the risk of SAEs and any condition, psychiatric, substance abuse, or otherwise, that, in the opinion of the Investigator, would preclude informed consent, consistent follow-up, or compliance with any aspect of the study
21. Subject is the Investigator or any Sub-Investigator, research assistant, pharmacist, study coordinator, other staff or relative thereof directly involved in the conduct of the protocol.
22. Any treatment within 72 hours prior to inclusion
23. Prior participation in a clinical trial with SENS-111

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-08-2018
Enrollment:	32
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	SENS-111
Generic name:	histamine H4 receptor antagonist
Product type:	Medicine
Brand name:	Suprimal
Generic name:	Meclozine (dihydrochloride)

Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	23-05-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-06-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-07-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2018-000777-80-NL
CCMO	NL65239.056.18

Study results

Date completed:	23-11-2018
Actual enrolment:	34