Solriamfetol*s Effect on Cognitive Health in Apnea Participants During a Randomized Placebo-controlled Study (SHARP): a 5-Week Double-blind, Placebo-controlled, Randomized, Crossover, Multicenter Study of Solriamfetol in Improving Cognitive Function in Participants With Excessive Daytime Sleepiness Associated With Obstructive Sleep Apnea Plus Impaired Cognitive Function.

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Primary Objective: To evaluate the effect of solriamfetol on cognitive functioning using an objective measurement. Secondary Objective:To evaluate the effect of solriamfetol on cognitive functioning using a subjective endpoint

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Sleep disturbances (incl subtypes)
Study type	Interventional

Summary

ID

NL-OMON50853

Source
ToetsingOnline

Brief title
JZP110-405

Condition

- Sleep disturbances (incl subtypes)

Synonym
Excessive Daytime Sleepiness, Sleep Apnea

Research involving
Human

Sponsors and support

Primary sponsor: Jazz Pharmaceuticals Inc.
Source(s) of monetary or material Support: Jazz Pharmaceuticals Inc.

Intervention

Keyword: Cognitive Function, Sleep Apnea, Solriamfetol

Outcome measures

Primary outcome

Difference in DSST means from the average of the 2- and 4-hour scores at

Baseline (Visit 3) to the average of the 2- and 4-hour postdose scores

(at Visit 5 and Visit 8) between solriamfetol and placebo.

Secondary outcome

1. Difference in overall BC-CCI score means from Baseline (Visit 3) to the end

of double-blind treatment period (Visit 5 and Visit 8) between

solriamfetol and placebo

2.

- Difference in DSST means from the average of the 2-, 4-, 6-, and 8-hour

scores at Baseline (Visit 3) to the average of 2-, 4-, 6-,

and 8-hour scores postdose (at Visit 5 and Visit 8) between solriamfetol and

placebo

- Difference in DSST means from each of the 2-, 4-, 6-, and 8- hour DSST RBANS sores at Baseline (Visit 3) to each of the corresponding 2-, 4-, 6-, and 8-hour postdose (at Visit 5 and Visit 8) DSST RBANS scores between solriamfetol and placebo

3. Safety and tolerability evaluations will be determined by the occurrence of and/or changes in:

• Incidence and severity of TEAEs

• Vital signs

• C-SSRS

Study description

Background summary

Obstructive sleep apnea is a sleep problem that happens when muscle and soft tissue in the throat blocks the airways and makes it difficult to breathe while asleep. People with obstructive sleep apnea may have a lower quality of sleep at night, which can mean they are very sleepy in the daytime. Daytime sleepiness can reduce mental function, including the ability to learn, think, concentrate, remember things, solve problems, or make decisions.

The study drug, solriamfetol, is a tablet taken by mouth. It is used to improve wakefulness in people with obstructive sleep apnea. Solriamfetol has been approved by the European Medicines Agency (EMA) and the United States Food and Drug Administration (FDA) for doctors to prescribe outside clinical trials for people with obstructive sleep apnea who still feel very sleepy in the daytime, despite using other standard therapies. Solriamfetol does not treat the underlying cause of obstructive sleep apnea, and does not take the place of other therapies, such as continuous positive airway pressure (CPAP).

The use of solriamfetol for improving mental function is investigational.

Study objective

Primary Objective:
To evaluate the effect of solriamfetol on cognitive functioning using an objective measurement.
Secondary Objective:
To evaluate the effect of solriamfetol on cognitive functioning using a subjective endpoint

Study design

The study is designed as a prospective, multicenter, 2-arm, randomized, double-blind, placebo-controlled interventional crossover trial of solriamfetol (75 mg titrated to 150 mg after 3 days) or matched placebo, then continued for a 2 week period total before completing a 1-week washout followed by the crossover period. Study intervention will be administered in a balanced 2 × 2 Latin square design, where half of the participants will receive placebo first and half of the participants will receive solriamfetol first.

Intervention

Subjects will be randomized 1:1 to solriamfetol versus placebo. Subjects will take either placebo or solriamfetol for two weeks, then have a one week washout period and then switch to the other e.g. subject taking solriamfetol in first two weeks will take placebo during the second two week period, and vice versa. Both solriamfetol and placebo will be administered orally, once a day. The dose of solriamfetol will be 75 mg to begin with and then uptitrated to 150mg

Study burden and risks

Previous clinical studies provide compelling evidence that solriamfetol has robust wake-promoting efficacy and a predictable safety profile that can be characterized, monitored and managed through routine clinical practice measures. Solriamfetol has a comprehensive clinical efficacy and safety database (including postmarketing experience) comprising healthy participants and those with EDS associated with OSA and narcolepsy, with a consistent safety profile across conditions. The benefit/risk profile is favorable in participants with OSA and narcolepsy, which supported the approval of doses up to 150 mg in each of these conditions. In the proposed trial, we will be targeting a final dose of 150 mg. This dose showed the highest level of improvement in wakefulness and reduction in sleepiness during the pivotal trials. The overall safety finding in participants taking the 150 mg dose was not significantly different from the 75 mg dose, and based on the titration schedule in clinical studies, the data from pivotal trials with solriamfetol

(Studies 14-004 and 14-005) support the initiation of solriamfetol at 75 mg once daily.
Potential safety risks with the use of solriamfetol are serious psychiatric events, increases in BP and HR, and a potential for abuse. The risks to participants are expected to be similar to those seen in prior clinical studies. Adverse events (AEs) following a single dose have generally been transient and mild to moderate.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Age and Sex
1. Male or female between 18 (or the legal age of consent in the jurisdiction in which the study takes place) and 65 years of age, inclusive.

Type of Participant and Disease Characteristics
2. Diagnosis of OSA according to International Classification of Sleep Disorders, Third Edition criteria.
3. Participant report (with clinician concurrence) of at least 1 of the following primary OSA therapy criteria:
• Consistent number of hours of primary PAP therapy use (with downloadable history) for OSA on at least 5 nights/week for at least 1 month prior to Baseline (with or without prior OSA surgical intervention), OR
• No current use of PAP therapy for at least 1 month prior to Baseline but a history of at least 1 month of attempting to use PAP as the primary OSA therapy with at least 1 documented adjustment that was made in an attempt to optimize the therapy (with or without prior OSA surgical intervention), OR
• History of a surgical intervention intended to treat OSA symptoms (with or without current PAP use as primary OSA therapy).
4. The participant has an age-corrected scaled score <= 8 on the DSST Wechsler Adult Intelligence Scale, Fourth Edition (WAIS-IV) at the Screening visit.
5. British Columbia-Cognitive Complaints Inventory >= 9 at Screening and Baseline.
6. Epworth Sleepiness Scale (ESS) score > 10 at Screening and Baseline.
7. Usual nightly total sleep time of >= 6 hours.
Weight
8. Body mass index from 18.5 to < 40 kg/m2.
Sex and Contraceptive/Barrier Requirements
9. Male and female Participants
a. Male participants:
Male participants are eligible to participate if they agree to the following during the study intervention period and for at least 14 days after the last dose of study intervention:
• Refrain from donating sperm
PLUS, either:
• Be abstinent from heterosexual intercourse as their preferred and usual lifestyle (abstinent on a long-term and persistent basis) and agree to remain abstinent
OR
• Must agree to use contraception/barrier as detailed below
• Agree to use a male condom with female partner use of an additional highly effective contraceptive method with a failure rate of < 1% per year as described in Appendix 5 Contraceptive and Barrier Requirements when having sexual intercourse with a women of childbearing potential (WOCBP) who is not currently pregnant.
b. Female participants:
• A female participant is eligible to participate if she is not pregnant or breastfeeding, and 1 of the following conditions applies:
* Is a woman of nonchildbearing potential (WONCBP) as defined in

Appendix 5 Contraceptive and Barrier Guidance
OR
* Is a WOCBP and using a contraceptive method that is highly effective (with a failure rate of < 1% per year), as described in 0 Contraceptive and Barrier Guidance during the study intervention period and for at least 14 days after the last dose of study intervention. The investigator should evaluate the potential for contraceptive method failure (eg, noncompliance, recently initiated) in relationship to the first dose of study intervention.
• A WOCBP must have a negative highly sensitive pregnancy test (urine or serum as required by local regulations) within the Screening/Baseline period (once at the time of Screening for participation in the study and again at the time of the study Baseline assessment) before the first dose of study intervention, see Section 8.4.5 Pregnancy Testing.
• Additional requirements for pregnancy testing during and after study intervention are located in Section 8.4.5.
• The investigator is responsible for review of medical history, menstrual history, and recent sexual activity to decrease the risk for inclusion of a woman with an early undetected pregnancy.
Informed Consent
10. Capable of giving signed informed consent as described in Section 10.1.3, which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol.

Exclusion criteria

1. Female participants who are pregnant, nursing, or lactating.
2. Usual bedtime later than 1 AM (0100 hours).
3. Occupation requiring nighttime or variable shift work.
4. Unable to understand or perform DSST test per investigator's judgement.
6. Diagnosis of another sleep disorder (other than OSA) including: circadian rhythm sleep disorders, narcolepsy, restless legs syndrome determined by participant sleep history.
7. Presence of acutely unstable major depression or current major depressive episode as based on the judgement of the investigator.
8. Participants with active clinically significant illness, including endocrine, neoplastic, gastrointestinal, hematological, hepatic, immunologic, metabolic, neurological, pulmonary, and/or renal disease, and/or surgical history which could interfere with the study efficacy, safety, conduct or the ability of the participant to complete the study based on the judgement of the investigator, or place the participant at risk during the trial or compromise the study objectives.
9. History or presence of any other clinically relevant medical,

behavioral, or psychiatric disorder other than OSA that is associated with an impact on cognitive function; including history or presence of neurodegenerative condition (eg, mild cognitive impairment due to Alzheimer's), autism, vascular dementia, active suicidal ideation, that could affect the safety of the participant or interfere with study efficacy, safety, conduct or the ability of the participant to complete the trial based on the judgment of the investigator.
10. History or presence of bipolar disorder, bipolar related disorders, schizophrenia, schizophrenia spectrum disorders, or other psychotic disorders according to Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria.
11. History of bariatric surgery within the past year or a history of any gastric bypass procedure.
13. Presence of renal impairment or calculated creatinine clearance < 60 mL/minute.
14. Clinically significant ECG abnormality in the opinion of the investigator.
15. Presence of significant cardiovascular disease including but not limited to: myocardial infarction within the past year, unstable angina pectoris, symptomatic congestive heart failure (ACC/American Heart Association stage C or D), revascularization procedures within the past year, uncontrolled atrial fibrillation, ventricular cardiac arrhythmias requiring automatic implantable cardioverter defibrillator or medication therapy, uncontrolled hypertension (as defined by Centers for Disease Control and Prevention), systolic blood pressure >= 155 mmHg or diastolic blood pressure >= 95 mmHg (at Screening or Baseline), or any history of cardiovascular disease or any significant cardiovascular condition that in the investigator's opinion may jeopardize participant safety in the study.
16. Laboratory value(s) outside the laboratory reference range that is considered to be clinically significant by the investigator (clinical chemistry, hematology, and urinalysis). NOTE: Screening labs may be repeated once.
17. Hypothyroidism or hyperthyroidism, unless stabilized by appropriate medication for at least 3 months prior to Screening (a normal thyroidstimulating hormone is required prior to Randomization at Baseline).
Prior/Concomitant Therapy
18. Use of any over-the-counter (OTC) or prescription medications that could affect the evaluation of EDS within a time period prior to the Baseline visit corresponding to at least 5 half-lives of the drug(s) or planned use of such drug(s) at some point throughout the duration of the 5-week double-blind treatment period. Examples of excluded medications include OTC sleep aids, stimulants (eg methylphenidate, amphetamines, modafinil, and armodafinil), sodium oxybate, pemoline, pitolisant, bupropion, trazodone, vortioxetine, duloxetine, tricyclic antidepressants, hypnotics, benzodiazepines, pseudoephedrine, barbiturates, and opioids. Medications should be discontinued such that,

in the opinion of the investigator, the participant has returned to his/her Baseline level of daytime sleepiness at least 7 days prior to the Baseline visit.
19. Current or recent (within the past 2 years) diagnosis of a moderate or severe substance use disorder (excluding caffeine) according to DSM-5 criteria, or seeking treatment for a substance-related disorder. Nicotine use disorder is excluded only if it has an effect on sleep (ie, a participant who routinely awakens at night to smoke).
25. History of phenylketonuria or history of hypersensitivity to phenylalanine-derived products.
26. Currently receiving MAO inhibitors or having had received MAO inhibitors for 14 days prior to the Baseline visit.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-06-2021
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Sunosi
Generic name:	Solriamfetol
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	13-04-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-06-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-01-2022
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	EUCTR2020-004243-92-NL
ClinicalTrials.gov	NCT04789174
CCMO	NL76973.056.21