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Efficacy and tolerability of tasipimidine in sleepless patients

Submission date 09/08/2023	**Recruitment status** Recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 15/08/2023	**Overall study status** Ongoing	
Last Edited 28/01/2025	**Condition category** Nervous System Diseases	

Plain English Summary
Background and study aims
Insomnia (sleeplessness) disorder is characterised by difficulties in initiating or maintaining sleep and can cause impairment in daytime functioning. It is a common condition, with an approximate general population prevalence of 10%. Cognitive behavioural therapy is currently recommended for insomnia as a first-line treatment, but not all insomnia patients benefit from it, and it might not be available for all. The available sleep medications can be modest in efficacy, can have abuse potential and have a risk of tolerance. Based on the mode of action, tasipimidine is expected to decrease arousal and cause sedation. The purpose of this study is to see if tasipimidine will help in the treatment of insomnia and how safe it is to use in people.

Who can participate?
Adult patients with insomnia aged between 18 and 65 years old

What does the study involve?
The patients will be randomised either to tasipimidine or a dummy treatment group. The study has a screening period (up to 5 weeks), a treatment period (3 consecutive days and nights) and a post-treatment period (up to 10 days). The study visits will take place in sleep centres. A sleep polysomnography (PSG) recording will be done on 2 screening nights and 2 treatment nights. The PSG will be done using equipment that records brain waves and other sleep parameters. Also, other health exams and tests will be taken during study visits.

What are the possible benefits and risks of participating?
Tasipimidine may favour sleep but in this study, the study drug will be administered for 3 nights only. Patients may also experience benefits due to getting information on their health. Participation may help other insomnia people in the future. There are no costs to participants to be in the study.
Tasipimidine has been well tolerated in a study with healthy volunteers. Based on that study and the mode of action, tasipimidine may cause dizziness when standing up. To minimise the risk associated with taking part in the study, patients are frequently monitored and evaluated for any side effects.

Where is the study run from?
Sleep centres in Finland, Poland and Germany

When is the study starting and how long is it expected to run for?
October 2022 to May 2025

Who is funding the study?
Orion Corporation (Finland)

Who is the main contact?
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Additional identifiers

EudraCT/CTIS number
2022-502483-21-00

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
3110012

Study information

Scientific Title
Efficacy and tolerability of tasipimidine after 3 repeated bed-time doses in patients with insomnia disorder

Acronym
UNITAS

Study hypothesis
Tasipimidine is superior to placebo assessed in patients with insomnia disorder.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 24/05/2023, National Committee on Medical Research Ethics (Tukija) (Tukija, Valvira P.O. Box 43, Helsinki, FI-00521, Finland; +358 295209111; info@tukija.fi), ref: 2022-502483-21-00

2. Approved 29/05/2023, Office for Registration of Medicinal Products, Medical Devices and Biocidal Products (Al. Jerozolimskie 181C, Warsaw, 02-222, Poland; +48224921100; urpl@urpl.gov.pl), ref: 2022-502483-21-00

3. Approved 11/07/2024, Ethics Committee of the Bavarian State Medical Association (Mühlbaurstraße 16, Munich, 81677, Germany; +49894147165; ethikkommission@blaek.de), ref: B_01899

Study design
Multisite interventional double-blind randomized placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Safety, Efficacy

Participant information sheet
See study outputs table

Condition
Insomnia

Interventions
The study drug, tasipimidine, is a highly specific α2 adrenoceptor agonist, selective for α2A receptor subtype. In experimental animals, it induces typical α2-adrenoceptor agonist effects like sedation, analgesia, and relief of anxiety. In humans, it is expected to decrease arousal and cause sedation. In this study, the effect of tasipimidine on sleep is investigated in a sleep laboratory setting.

Three escalating adaptive dose levels of tasipimidine are planned to be administered to 3 sequential cohorts of subjects and the placebo will be randomised into each dose level in a 1:3 ratio. Subjects will be allocated at random to tasipimidine and placebo groups by the IVRS system. After each cohort, the Data and Safety Monitoring Board will evaluate the data and agree on the dose level for the next cohort. The study drug is given by the study site personnel as an oral liquid on 3 consecutive nights. Study subjects will stay at the study site for 3 consecutive nights and days from the evening of Day 1 until the afternoon of Day 4.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic, Pharmacodynamic, Dose response, Pharmacogenetic, Pharmacogenomic

Phase
Phase II

Drug/device/biological/vaccine name(s)
Tasipimidine

Primary outcome measure
Effect on sleep is measured using sleep polysomnography measurement on 2 baseline nights and on 2 treatment nights

Secondary outcome measures

1. Safety and tolerability measured by collecting adverse events throughout the study, vital signs on study visits, morning sleepiness scale after each of the 3 nights, safety laboratory tests on screening, Day 1, Day 4 and end-of-study visit
2. Pharmacokinetics (PK) measured by collecting samples for PK analysis during Night 3 and Day 4

Overall study start date
01/10/2022

Overall study end date
31/05/2025

Eligibility

Participant inclusion criteria
1. Signed informed consent (IC) for participation in the study
2. Male or female subjects aged between 18 and 65 years (inclusive) at the screening visit
3. Insomnia disorder according to Diagnostic and Statistical Manual of Mental Disorders, 5th Edition Text Revision (DSM-5-TR®)
4. Self-reported history of the following on at least 3 nights per week and for at least 3 months prior to the screening: ≥ 30 minutes to fall asleep, subjective total sleep time (sTST) ≤ 6 hours.
5. Insomnia Severity Index© (ISI©) score ≥ 15
6. Usual bedtime between 21:00 and 02:00
7. Regular time in bed between 6 and 9 hours
8. Meeting the following sleep parameter criteria on the 2 screening PSG nights: mean latency to persistent sleep (LPS) ≥ 25 minutes (with none of the 2 nights < 15 minutes) and mean total sleep time (TST) ≤ 6 h
9. Female subjects with fertile male partners, and male subjects with female partners of childbearing potential, must adhere to a highly effective form of contraception, if sexually active and not permanently sterilised. Additionally, women who are postmenopausal (1 year since the last menstrual cycle) are considered not to be reproductive and can be included.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex
Both

Target number of participants
The planned number of subjects is 96, 32 patients in each cohort.

Participant exclusion criteria

1. A predictable poor compliance or inability to understand and comply with protocol requirements, instructions and protocol-stated restrictions, or communicate well with the investigator
2. Body mass index below 18.5 or above 40.0 kg/m2
3. Self-reported usual daytime napping ≥ 1 hour per day, and ≥ 3 days per week
4. Shift work within 2 weeks prior to the screening visit, or planned shift work during the study
5. Travel across ≥ 3 time zones within 2 weeks prior to the screening visit, or planned travel across ≥ 3 time zones during the study
6. Use of medications with known relevant alpha-2 AR affinity (e.g. mirtazapine, mianserine, dexmedetomidine, clonidine, guanfacine or tizanidine) or known strong or moderate CYP2D6 inhibitors (e.g. paroxetine, fluoxetine, bupropion, quinidine) within 14 days or 5 times the half-life, whichever is longer, prior to the 1st screening PSG
7. Use of benzodiazepines, z-drugs (zolpidem, zopiclone, eszopiclone, zaleplon), melatonin, sedative H1 antagonists, sedative antidepressants (e.g. doxepine and trazodone), orexin receptor antagonists (e.g. daridorexant) or antipsychotics within 14 days or 5 times the halflife, whichever is longer, prior to 1st screening PSGs
8. Use of amphetamine derivatives like methylphenidate, dexamphetamine and lisamphetamine within 14 days, or 5 times the half-life, whichever is longer, prior to the 1st screening PSG
9. Use of other CNS-active drugs, including over-the-counter or herbal medicines, for 14 days or 5 times the half-life, whichever is longer, prior to the 1st screening PSG
10. Start other new chronic medication within 14 days or 5 times the half-life, whichever is longer, prior to the 1st screening PSG
11. Cognitive behavioural therapy (CBT) for any indication is allowed only if the CBT started at least 1 month prior to the 1st screening PSG and the subject agreed to continue the CBT throughout the study
12. Any lifetime history of sleep-related breathing disorders, including chronic obstructive pulmonary disease and sleep apnoea
13. Acute or unstable psychiatric conditions as judged by the investigator (including but not restricted to current bipolar disorder, schizophrenia or obsessive-compulsive disorder) that are diagnosed by the Mini International Neuropsychiatric Interview© (MINI©) or that require pharmacological treatment for these disorders. N.B.: subjects with a history of major depressive disorder or anxiety disorder that are currently stable, and without requiring pharmacological treatment are eligible
14. Positive answer to item 4 or 5 on the Colombia-Suicide Severity Rating Scale (C-SSRS) or current risk of suicide based on the investigator's judgement at the screening visit
15. Diagnosis of alcohol or substance use disorder within 2 years prior to the screening visit or inability to refrain from drinking alcohol for at least 3 consecutive days.
16. Myocardial infarction or other clinically significant ischemic cardiac disease, heart failure, sick sinus syndrome or arrhythmia tendency within the past 2 years
17. History of clinically significant orthostatic hypotension, syncope or syncopial attacks within the past 2 years
18. Any other clinically significant cardiovascular, pulmonary, gastrointestinal, hepatic, renal, neurological (e.g. epilepsy or dementia) or psychiatric disorder or any other major concurrent illness that in the opinion of the investigator may interfere with the interpretation of the study results or constitute a health risk for the subject if he/she takes part in the study
19. Heavy tobacco use (at least one pack of cigarettes a day or inability to refrain from smoking during the night)
20. Caffeine consumption ≥ 600 mg per day or regular caffeine consumption after 4 p.m.
21. Supine HR < 50 bpm or > 100 bpm after a 5-minute rest at the screening visit
22. Systolic blood pressure (SBP) < 100 or > 160 mmHg or diastolic blood pressure (DBP) < 50 or

> 100 mmHg after a 5-minute rest at screening visit
23. Orthostatic hypotension (decrease of ≥ 20 mmHg for SBP or decrease of ≥10 mmHg for DBP) or dizziness in orthostatic test at screening visit
24. Abnormal 12-lead ECG finding of clinical relevance at the screening visit, (after 5 min rest in the supine position, confirmed by a repeat measurement) for example: QTc (calculated through the Fridericia's formula) repeatedly > 450 ms in males or > 470 ms in females at the screening visit. Pacemaker rhythm as such does not need to lead to exclusion. (If the QTc interval measured by the ECG machine algorithm is > 450 ms, 2 additional recordings will be done and QTcF values confirmed) -2° or 3° AV block.
25. AST and/or ALT > 2 × ULN and/or direct bilirubin > 1.5 × ULN
26. Positive urine drug screen or presence of alcohol in an exhaled breath at screening visit, screening PSG nights or on Day 1
27. Any other abnormal value in laboratory tests, vital signs or 12-lead ECG which may in the opinion of the investigator interfere with the interpretation of the study results or cause a health risk for the subject if he/she takes part in the study
28. Pre-planned elective surgery for the study period
29. Known hypersensitivity to the active substance or to any of the excipients of the study treatment
30. Pregnant or lactating females
31. Blood donation or loss of a significant amount of blood within 60 days prior to the screening
32. Participation in a drug study within 60 days prior to the screening
33. Periodic limb movement disorder with arousal index (PLMAI) ≥ 15/h (assessed on the 1st screening PSG night), restless legs syndrome, circadian rhythm disorder, REM behaviour disorder, or narcolepsy
34. Apnoea/hypopnea index (AHI) ≥ 15/h according to American Academy of Sleep Medicine criteria or event associated with blood oxygen saturation level by pulse oximetry (SpO2) < 80%, as assessed on the 1st screening PSG night
35. Any other condition that in the opinion of the investigator may interfere with the interpretation of the study results or constitute a health risk for the subject if he/she takes part in the study

Recruitment start date
28/07/2023

Recruitment end date
30/04/2025

Locations

Countries of recruitment
Finland

Germany

Poland

Study participating centre
Terveystalo Helsinki Uniklinikka
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ROR
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Funder(s)

Funder type
Industry

Funder Name
Orion Corporation

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
31/05/2026

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from https://www.orion.fi/en/sustainability/ethical-business/research-development-ethics-policy/sharing-clinical-data/

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet		16/12/2022	15/08/2023	No	Yes