Single-center, randomized, double-blind, single-dose, 3-way crossover study to compare the effects of daridorexant and placebo on postural stability, the auditory awakening threshold, and cognitive function in the middle-of-the-night following evening administration to healthy adult and elderly subjects

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To evaluate the pharmacodynamic (PD) effects of daridorexant 25mg, 50mg, and placebo in the middle-of-the-night.

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

Summary

ID

NL-OMON51304

Source
ToetsingOnline

Brief title
Study investigating the effects of daridorexant in healthy subjects

Condition

- Sleep disturbances (incl subtypes)

Synonym

Insomnia, Sleeplessness

Research involving
Human

Sponsors and support

Primary sponsor: Idorsia Pharmaceuticals Ltd
Source(s) of monetary or material Support: Industry

Intervention

Keyword: Body sway, Daridorexant, Insomnia, Orexin

Outcome measures

Primary outcome

Pharmacodynamic endpoints

Secondary outcome

Safety and tolerability endpoints

Study description

Background summary

Sleep-promoting drugs should ideally induce sleep while having no considerable effects on postural stability when getting out of bed during the night, or when waking up in the morning. In addition, it is a common safety concern with CNS-depressant drugs that they may decrease the ability of subjects to be awakened by external stimuli such as a fire alarm. Daridorexant has been approved for medical use in the United States and Europe and is sold under the brand name registered QUVIVIQ to treat insomnia. This study will investigate the side effects of Daridorexant when subjects are abruptly woken in the middle of the night.

Study objective

To evaluate the pharmacodynamic (PD) effects of daridorexant 25mg, 50mg, and placebo in the middle-of-the-night.

Study design

Single-center, double-blind, randomized, placebo-controlled, single-dose, 3-way crossover Phase 1 study.

Intervention

Daridorexant (25mg and 50 mg) and placebo

Study burden and risks

As this study is not conducted in the target population for daridorexant, there are no anticipated clinical benefits for participants beyond the thorough medical check-up that each subject will undergo prior to receiving treatments and at the end of the study. The selection of healthy subjects is justified on the basis that the nighttime PD variables can be investigated accurately in this population, without interferences from concomitant diseases or medication. In addition, results can be compared to previous findings obtained in healthy subjects when the PD of daridorexant were evaluated at different doses following daytime administration. However, effects on nighttime PD of patients with insomnia cannot be derived from this study. Provided the protocol is adhered to, the exclusion criteria, careful observation, and medical management will minimize any associated risk in this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Signed informed consent in a language understandable to the subject prior to any study-mandated procedure.
2. Male and female subjects aged >= 18 years at Screening (18 subjects must be >= 65 years).
3. Woman of childbearing potential (WoCBP) who has a negative serum pregnancy test at Screening and a negative urine pregnancy test on Day 1 pre-dose. She must agree to use consistently and correctly (from Screening, during the entire study, and for at least 5-7 days after last study treatment administration) an acceptable method of contraception with a failure rate of < 1% per year, be sexually inactive, or have a vasectomized partner. If a hormonal contraceptive is used, it must be initiated at least 1 month before first treatment administration.
4. Woman of non-childbearing potential, i.e., postmenopausal (defined as 12 consecutive months with no menses without an alternative medical cause, confirmed by a follicle-stimulating hormone [FSH] test), with previous bilateral salpingectomy, bilateral salpingo-oophorectomy or hysterectomy, or with premature ovarian failure (confirmed by a specialist), XY genotype, Turner syndrome, or uterine agenesis.
5. Body mass index (BMI) of 18.0 to 35.0 kg/m2 (inclusive) at Screening.
6. Ability to communicate well with the investigator, in a language understandable to the subject, and to understand and comply with the study requirements.
7. Usual bedtime between 21:30 and 00:30 and usual sleep duration of at least 6 h.

Exclusion criteria

1. Known hypersensitivity to daridorexant, or treatments of the same class, or any of its excipients.
2. History of narcolepsy.
6. Any known factor or disease (e.g., unstable medical condition, significant medical disorder, or acute illness) that might interfere with subject*s safety, study conduct, or interpretation of the results, such as: history of non-compliance with medical regimen; history of hearing impairment, psychiatric disease; or neurological disorder that may impact sleep, motor performance, or

cognition, including Parkinson disease, predementia, dementia, other neurodegenerative disorder, and stroke.
16. Shift work within 2 weeks prior to Screening, or planned shift work during the study.
17. Travel across >= 3 time zones within 1 week prior to Screening, or planned travel across >= 3 time zones during the study.
18. Previous (i.e., within 2 weeks prior to first study treatment administration) and ongoing treatment with any prescribed central nervous system (CNS)-active medications, and/or diuretics that would affect nighttime rest, and/or moderate to strong cytochrome P450 (CYP)3A4 inhibitors or inducers.
19. Mini Mental State Examination (MMSE) score < 25 in subjects >= 65 years at Screening.

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	05-01-2023
Enrollment:	36
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	QUVIVIQ
Generic name:	Daridorexant
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	28-11-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-12-2022
Application type:	First submission
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	EUCTR2022-002922-28-NL
CCMO	NL83038.056.22

Study results

Date completed:	15-04-2023
Results posted:	24-05-2024

First publication
16-04-2024