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Daridorexant for Alzheimer's disease prevention

Submission date	Recruitment status	[X] Prospectively registered
06/10/2025	Recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
07/10/2025	Ongoing	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
07/10/2025	Mental and Behavioural Disorders	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Alzheimer’s disease starts many years before symptoms appear, with harmful changes in the brain like the buildup of amyloid plaques and tau tangles. Researchers are looking for ways to slow or prevent these changes. This study is testing a sleep medication called daridorexant, which may help clear these proteins, reduce brain inflammation, and improve thinking skills. The goal is to see if daridorexant could help prevent Alzheimer’s disease.

Who can participate?
People aged 50 to 90 years who are in generally good health and do not have Alzheimer’s disease or any other form of dementia may be eligible. You don’t need to have insomnia to take part. The study team will review your health and medications to make sure you meet all the requirements.

What does the study involve?
Participants will take either daridorexant or a placebo (a look-alike pill with no active ingredient) every night for one year, 30 minutes before bedtime. Before starting, there will be a screening visit to check eligibility, followed by a baseline evaluation with memory tests, questionnaires, a blood draw, and an optional lumbar puncture. Sleep will be tracked for a week using a headband device. These same tests will be repeated at the end of the year. There will also be safety check-ins by phone and in-person visits at 3, 6, and 9 months.

What are the possible benefits and risks of participating?
There is no guaranteed personal benefit from joining the study, but participants may feel good about helping advance Alzheimer’s research. Some people might experience better sleep or improved brain health, but these effects are not certain. Risks include mild side effects from the drug (like sleepiness, headache, or nausea), discomfort from blood draws or questionnaires, and possible headaches from the optional lumbar puncture. There’s also a small risk of a privacy breach.

Where is the study run from?
The study is being conducted at the StoP-Alzheimer Centre, part of the Douglas Mental Health University Institute – Research Center in Montreal, Quebec, Canada.

When is the study starting and how long is it expected to run for?
October 2023 to December 2028.

Who is funding the study?
Weston Family Foundation (Canada)

Who is the main contact?
Jennifer Tremblay-Mercier, MSc, prevenir.alzheimer@douglas.mcgill.ca

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
DARAD2025

Study information

Scientific Title
Double blind clinical trial of Daridorexant (dual orexin receptor antagonist) for Alzheimer's disease prevention

Acronym
PAD-DORA

Study objectives
This study will evaluate whether daridorexant, a sleep medication (Dual Orexin Receptor Antagonist (DORA)), can support brain health by promoting the clearance of proteins linked to the development and progression of Alzheimer's disease.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 26/09/2025, Centre intégré universitaire de santé et de services sociaux de l'Ouest-de-l'Île-de-Montréal Research Ethics Board (6875 Lasalle blvd, Montreal, H4H 1R3, Canada; +1 514 761-6131; recherche.comtl@ssss.gouv.qc.ca), ref: 2025-1180

Study design
Single-site double-blind randomized placebo-controlled interventional study

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied

Prevention of Alzheimer's disease in participants without Alzheimer's disease dementia, experiencing sleep problems or not

Interventions
240 participants will be randomized (1:1). There are 2 arms. One experimental arm (daridorexant 50 mg) and one placebo arm. Study drug (daridorexant 50 mg or placebo) will be taken orally each night 30 minutes before bedtime for 1 year (the duration of the study).

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Daridorexant (Quviviq) 50 mg DIN 02537443

Primary outcome(s)
Biological progression as measured by p-tau217/np-tau217 ratio in plasma. Time Frame: baseline up to estimated 12 months

Key secondary outcome(s))
1. Biological progression as measured by p-tau181/np-tau181 ratio in plasma. Time Frame: baseline up to estimated 12 months
2. Biological progression as measure by Aβ42/Aβ40 ratio in plasma. Time Frame: baseline up to estimated 12 months
3. Cognitive progression as measured with a modified version of the Preclinical Alzheimer Cognitive Composite Score. Time Frame: baseline up to estimated 12 months
4. Cognitive progression as measured with the XpressO MoCA medical screening tool. Time Frame: baseline up to estimated 12 months
5. Aβ42/Aβ40 ratio in cerebrospinal fluid in a subset of participants. Time Frame: baseline up to estimated 12 months
6. Sleep efficiency as measured by EEG recordings. Time Frame: baseline up to estimated 12 months.
7. Astroglial activation and astrocytosis as measured by glial fibrillary acidic protein (GFAP) levels in plasma. Time Frame: baseline up to estimated 12 months.
8. Biological progression as measured by p-tau181/np-tau181 ratio at 3 months, in plasma. Time Frame: baseline to estimated 3 months
9. Biological progression as measured by p-tau217/np-tau217 ratio at 3 months, in plasma. Time Frame: baseline to estimated 3 months

Completion date
15/12/2028

Eligibility

Key inclusion criteria
1. Without dementia as determined by: MoCA >21 or MMSE > 24 or Clinical Dementia Rating <1
2. Minimum of 6 years of formal education

3. Stable psychoactive medication for 1 month prior to screening with no intention to change dose during treatment period
4. Capacity to provide written consent in English or French

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
50 years

Upper age limit
90 years

Sex
Male

Key exclusion criteria
1. Clinical diagnosis of major neurocognitive disorder
2. Unstable psychiatric condition
3. Clinically significant active suicidal ideations
4. Unstable medical condition in the opinion of the investigator.
5. Known or suspected history of drug or alcohol dependence or abuse within one year of the screening visit
6. Currently taking a DORA
7. Allergy or significant adverse reaction to DORA
8. Use of benzodiazepines or z-drugs > 2 times per week in the last month.
9. Use of major and moderate CYP3A4 inducers and inhibitors
10. Use of strong central nervous system depressants, opioids, strong analgesics, antipsychotics, sedative antidepressants.
11. Active use of cholinesterase inhibitors or memantine
12. Women who are breast feeding or pregnant
13. Severe obstructive sleep apnea (OSA)
14.Clinically significant non-treated rapid eye movement (REM) sleep behavior disorder, restless leg syndrome or parasomnia;
15. Diagnosis of narcolepsy

Date of first enrolment
14/10/2025

Date of final enrolment
15/12/2027

Locations

Countries of recruitment
Canada

Study participating centre
StoP-Alzheimer Centre (Douglas Mental Health University Institute - Research Centre)
6875, Lasalle blvd
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Canada
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Sponsor information

Organisation
Douglas Mental Health University Institute

ROR
https://ror.org/05dk2r620

Funder(s)

Funder type
Charity

Funder Name
Weston Family Foundation

Alternative Name(s)
The Weston Family Foundation, Fondation de la famille Weston, WFF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Canada

Results and Publications

Individual participant data (IPD) sharing plan

Coded individual participant data will be shared through the StoP-Alzheimer Centre open science initiatives (Repository: registeredpreventad.loris.ca and via the Canadian Open Neuroscience Platform)

IPD sharing plan summary

Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes