ISRCTN17719546 https://doi.org/10.1186/ISRCTN17719546

Efficacy of rivastigmine transdermal patch in patients with mild cognitive impairment with Lewy bodies

Submission date
06/03/2024

Recruitment status
No longer recruiting

Registration date
14/03/2024

Overall study status
Completed

Last Edited
07/03/2024

Condition category
Nervous System Diseases

[ ] Prospectively registered
[X] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Acetylcholinesterase inhibitors (AChEIs) are a class of drugs that are proven to help improve cognitive (thinking) functions in dementia of Alzheimer's type and dementia of Lewy bodies. However, their effectiveness in patients with mild cognitive impairment (MCI), a pre-dementia stage, has not been proven by clinical studies. However, the result of these studies may not be generalisable to patients suffering from mild cognitive impairment with Lewy bodies (MCI-LB) since the participants of these studies were mainly suffering from Alzheimer's disease MCI (MCI-AD). Lewy body disease is suggested to have a more significant cholinergic deficit than Alzheimer's disease, which can explain the superior effectiveness of AChEIs in improving cognitive symptoms in patients with DLB over AD. It is possible that patients with MCI-LB might respond to AChEI better than patients with MCI-AD. One of the key obstacles in studying MCI-LB has been its diagnostic ambiguity. Research in the last two decades has established the specificity of REM sleep behaviour disorder (RBD) in predicting Lewy body disease. In recognising this, the recent research definition of MCI-LB stated that patients with MCI and RBD can be diagnosed as having MCI-LB. In other words, the diagnosis of RBD is a key feature that allows us to identify MCI-LB patients for clinical trials with high specificity. The rivastigmine transdermal patch is approved by the FDA to treat mild-to-moderate dementia of Alzheimer's type and mild-to-moderate dementia associated with Parkinson's disease. The drug is safe and generally well tolerated. The rivastigmine transdermal patch has a better side effect profile compared to an oral preparation. The aim of this study is to test the effectiveness of the rivastigmine transdermal patch at improving cognitive function, mood and anxiety symptoms and quality of life in patients with MCI-LB with RBD at 6 months.

Who can participate?
Patients aged 60 to 80 years old with LB-MCI and RBD

What does the study involve?
The transdermal patch will be started at a standard starting dose of 4.6 mg/24 hours. If the participant tolerates the treatment, the dosage will be increased to 9.5 mg/24 hours after 4 weeks and continued until the end of the trial. If the patient reports intolerable side effects with

the dosage of 9.5 mg/24 hours, the dosage is reduced back to 4.6 mg/24 hours after clinical assessment. If the patient cannot tolerate 4.6 mg/24 hours, the drug will be discontinued. The research nurse or clinician will demonstrate the proper use of the patch before the beginning of the trial. The researchers will provide the patient with a log sheet that allows them to collect the used patch according to the administration date. Using this method, the patient's compliance can be monitored. The researchers will also call the patients twice weekly to remind them of the proper medication use in the first 2 weeks and once every 2 weeks after that.

What are the possible benefits and risks of participating?
The possible benefits are improvements in the global cognitive function of patients with MCI-LB with RBD in 6 months. The side effects listed as having a frequency of 2% or more at the target dose (9.5 mg/24 hours) will be monitored. They are significant weight loss, nausea and vomiting, diarrhoea, abdominal pain, depression and anxiety, application site skin reaction, headache, dizziness, fatigue, falls, urinary tract infection, and agitation. Adverse effects that are theoretically plausible but not shown to have increased in clinical trials will also be monitored. These include bradycardia, gastric ulcer, gastrointestinal bleeding, urinary obstruction, and an increase in parkinsonism. The local skin reaction to the patch will also be monitored.

Where is the study run from?
The Chinese University of Hong Kong (Hong Kong)

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

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Dr Steven Wai Ho Chau, stevenwaihochau@cuhk.edu.hk

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Dr Steven, Wai Ho Chau

Contact details
7/F, Department of Psychiatry
Shatin Hospital
New Territories
Hong Kong
000000
+852 (0)9582 2342
stevenwaihochau@cuhk.edu.hk

Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
2022.607 - T

Study information

Scientific Title
Short-term efficacy of rivastigmine transdermal patch in patients with mild cognitive impairment with Lewy bodies (MCI-LB) and REM sleep behaviour disorder: a double-blind, randomized control study

Study objectives
Primary hypothesis:
Use of rivastigmine transdermal patch improves the global cognitive function of patients with mild cognitive impairment with Lewy bodies (MCI-LB) with REM sleep behaviour disorder (RBD) at 6 months.

Secondary hypotheses:
1. Use of rivastigmine transdermal patch improves the global cognitive function of patients with MCI-LB with RBD at 3 months.
2. Use of rivastigmine transdermal patch reduces depressive and anxiety symptoms of patients with MCI-LB with RBD at 6 months.
3. Use of rivastigmine transdermal patch improves the quality of life of patients with MCI-LB with RBD at 6 months.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 03/01/2024, Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee (8/F, Lui Che Woo Clinical Sciences Building, Prince of Wales Hospital, Shatin, New Territories, 000000, Hong Kong; +852 (0)35053935/21445926; crec@cuhk.edu.hk), ref: 2022.607-T

Study design
Single-centre interventional double-blinded randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
REM sleep behavior disorder and presence of probable LB-MCI

Interventions
Rivastigmine transdermal patch will be started at a standard starting dose of 4.6 mg/24 hours. If the subject tolerates the treatment, the dosage will be increased to 9.5 mg/24 hours after 4 weeks, and the researchers will continue this dosage until the end of the trial. If the patient reports intolerable side effects with the dosage of 9.5 mg/24 hours, the dosage is reduced back to 4.6 mg/24 hours after clinical assessment. If the patient cannot tolerate 4.6 mg/24 hours, the drug will be discontinued. The research nurse or clinician will demonstrate the proper use of the patch before the beginning of the trial.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Rivastigmine transdermal patch

Primary outcome(s)
Global cognitive function measured using the Hong Kong Montreal Cognitive Assessment (MoCA-HK) score between T1 (6 months post-treatment) and T0 (baseline assessment).

Key secondary outcome(s))
1. Global cognitive function measured using the Hong Kong Montreal Cognitive Assessment (MoCA-HK) between T0.5 (3 months post-treatment) and T0 (baseline assessment)
2. Depressive symptoms measured using the Patient Health Questionnaire-9 (PHQ-9) score between T1 and T0
3. Anxiety symptoms measured using the General Anxiety Disorder-7 (GAD-7) score between T1 and T0
4. Quality of life measured using the WHOQOL-BREF score (excluding the Environment domain) between T1 and T0

Completion date
01/03/2025

Eligibility

Key inclusion criteria
1. Aged 60 to 80 years old
2. Video-polysomnography confirmed diagnosis of RBD
3. Presence of probable LB-MCI as diagnosed by a specialist psychiatrist or neurologist according to the Research criteria for the diagnosis of prodromal dementia with Lewy bodies by the prodromal DLB Diagnostic Study Group
4. Capable of giving written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Senior

Lower age limit
60 years

Upper age limit
80 years

Sex
All

Key exclusion criteria
1. Presence of Parkinson’s disease, multi-system atrophy, or other neurodegenerative disorders
2. Condition that is contraindicated against rivastigmine patch: Presence of heart block, history of allergic reaction to rivastigmine, or drugs that have cross-hypersensitivity with rivastigmine
3. Conditions that render adverse events more likely: sick sinus syndrome, conduction defects (sino-atrial block, atrioventricular block), gastroduodenal ulcerative conditions (including those predisposed to such situations by concomitant medications), asthma or chronic obstructive pulmonary disease, urinary obstruction, and seizures
4. Body weight <50 kg
5. history of being treated with AChEI or other cognitive enhancers
6. Undergoing other structural, non-pharmacological cognitive-enhancing therapy
7. Other suspected causes of primary causes of cognitive impairment as suggested by clinical examination, blood tests and imaging investigations

Date of first enrolment
01/03/2024

Date of final enrolment
31/12/2024

Locations

Countries of recruitment
Hong Kong

Study participating centre
Sleep Clinic, Prince of Wales Hospital
30-32 Ngan Shing Street
Shatin
New Territories
Hong Kong
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Study participating centre

Sleep Assessment Unit, Shatin Hospital
33 A Kung Kok Street
Ma On Shan
Shatin
New Territories
Hong Kong
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Sponsor information

Organisation
Chinese University of Hong Kong

ROR
https://ror.org/00t33hh48

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan
The datasets will be published as a supplement to the results publication

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet			07/03/2024	No	Yes
Protocol file	version 1	07/11/2022	07/03/2024	No	No