A PHASE 1, TWO-PART RANDOMIZED, ADAPTIVE DRUG-DRUG-INTERACTION STUDY TO EVALUATE THE SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF DERAMCICLANE AND DEXTROMETHORPHAN, ALONE AND COMBINED, IN HEALTHY ELDERLY SUBJECTS

Published: 15-07-2021
Last updated: 05-04-2024

In this study we will investigate how safe the new compound deramciclane is, when it is given alone and in combination with the existing medication dextromethorphan (Part B), and how well it is tolerated when it is used by healthy elderly...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Dementia and amnestic conditions
Study type	Interventional

Summary

ID

NL-OMON49903

Source
ToetsingOnline

Brief title
Deramciclane and dextromethorphan DDI study in elderly subjects

Condition

- Dementia and amnestic conditions

Synonym
Behavioural and psychological symptoms of dementia

Research involving
Human

Sponsors and support

Primary sponsor: Exciva GmbH
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: DDI, Deramciclane, Dextromethorphan, Elderly

Outcome measures

Primary outcome

To assess the pharmacokinetics (PK) of multiple doses of deramciclane in

healthy elderly subjects

To assess the PK of multiple doses of dextromethorphan in healthy elderly

subjects

To assess the PK of multiple doses of dextromethorphan and deramciclane

combined in healthy elderly subjects

To assess the safety and tolerability of multiple doses of deramciclane,

dextromethorphan, and deramciclane combined with dextromethorphan,

in healthy elderly subjects

Secondary outcome

Not applicable.

Study description

Background summary

Deramciclane is a new compound that originally was being developed for the treatment of anxiety disorders. However clinical studies in patients were stopped early when the compound was not effective in reducing anxiety. Now deramciclane is repurposed for the possible treatment of behavioral symptoms of dementia, like agitation, aggression, disturbed emotions, and mood disturbances. These symptoms are very common in people with different forms of dementia, and are very stressful for both patients and their caregivers. Dextromethorphan is an existing medication and is mostly used as a cough suppressant in cough medication. But recently it is also being developed as compound for the treatment of diseases of the central nervous system (the brain). Dextromethorphan is broken down really fast by the liver by certain enzymes. One of the breakdown products is thought to cause the symptoms that occur with dextromethorphan overdose (hallucinations, agitation, or sedation). Therefore, in these studies into the effects of dextromethorphan on brain function, dextromethorphan is given in combination with quinidine. Quinidine slows down these liver enzymes, resulting in a slower breakdown of dextromethorphan. Deramciclane has a similar effect as quinidine, and it is expected to have additional therapeutic effects.It is thought that the combination treatment of deramciclane and dextromethorphan will reduce the behavioral symptoms in patients with dementia.

Study objective

In this study we will investigate how safe the new compound deramciclane is, when it is given alone and in combination with the existing medication dextromethorphan (Part B), and how well it is tolerated when it is used by healthy elderly participants. In Part A only deramciclane will be given, and in Part B both deramciclane and dextromethorphan will be given. We also investigate how quickly and to what extent deramciclane is absorbed, transported, and eliminated from the body. Deramciclane has been administered to humans before. In addition, it has been extensively tested in the laboratory and on animals.

Study design

Part A:
The study lasts a maximum of 8 weeks from the inspection to the follow-up check. For the research it is necessary that the volunteers stay in the research center for 2 periods; 1 period of 4 days (3 nights), and 1 period of 3 days (2 nights).
Day 1 is the first day of receiving the study drug. We expect the subjects to

be 2 days prior to the day of the first study drug administration at the study center (i.e. Day -2). You must then report at approximately 14:00 in the afternoon.

One leaves the research center on Day 2 of the research. For the second period, we expect the VW on Day 10. You must then report at approximately 14:00 in the afternoon. They leave the research center on Day 12 of the study. The arrival times can be adjusted

While at the research center, deramciclane is given as capsules by mouth with 240 milliliters (ml) of (tap) water. After taking the study drug, one of the researchers will inspect the hands and mouth. This is to check whether the study drug has been taken.

Mne will take deramciclane at home for a few days (from the evening on Day 2 until the morning of Day 10). At home you can eat and drink as usual, with the exception of a number of research-related restrictions. Please note that 48 hours (2 days) prior to each entry (Day -2 and Day 10), no beverages or food containing caffeine such as coffee, (ice) tea, cola, chocolate (milk), mocha may be consumed drinks/sweets, energy drinks.

One is requested to take the morning dose of deramciclane immediately after breakfast and the evening dose approximately 12 hours later. They are given instructions for dosing at home and a diary in which to record the time of each dose of deramciclane and any side effects. You will receive a text message and/or phone call twice a day as a reminder to take Deramciclane at home.

Part B:
The study takes a maximum of 9 weeks from the inspection to the follow-up check. For the research it is necessary to stay in the research center for 2 periods; 1 period of 7 days (6 nights), and 1 period of 3 days (2 nights).

Day 1 is the first day of receiving the study drug. We expect the volunteers to be 2 days prior to the day of the first study drug administration at the study center (this is Day -2). You must then report at approximately 14:00 in the afternoon.

The volunteer leaves the study center on Day 5 of the study. For the second period we expect the volunteers on Day 13.
You must then report at approximately 14:00 in the afternoon. They leave the research center on Day 15 of the study.

At the research center, dextromethorphan, and deramciclane, or placebo are given twice daily as capsules by mouth with 240 milliliters (ml) of (tap) water. After taking the study drug, one of the researchers will inspect your hands and mouth. This is to check whether the study drug has been taken.

Deramciclane and dextromethorphan will also be taken twice daily as capsules at home for several days (from the evening of Day 5 to the morning of Day 13). At home you can eat and drink as usual, with the exception of a number of research-related restrictions.

The morning dose of deramciclane and dextromethorphan is requested to be taken immediately after breakfast and the evening dose approximately 12 hours later. Dosing instructions are given and a diary is given in which to record the time of each dose of deramciclane and dextromethorphan and any side effects. You will receive a text or text message and/or phone call twice a day as a reminder to take deramciclane and dextromethorphan at home.

Intervention

Not applicable.

Study burden and risks

Blood draws may hurt or cause bruising. Using an indwelling cannula can sometimes cause inflammation, swelling, hardening of the artery, or blood clotting and bleeding around the puncture site. In some individuals, a blood draw can sometimes cause paleness, nausea, sweating, slow heart rate, or drop in blood pressure with dizziness or fainting.

All in all, we will no longer take 270 milliliters (ml) of blood from you. This amount does not cause any problems in adults. If the researcher does this necessary to ensure the safety of the participant, additional samples can be taken for any additional testing. If this happens, the total amount of blood drawn will be more than the amount indicated above.

To make a heart film, electrodes are placed on the arms, chest and legs. Prolonged use of these electrodes may cause skin irritation.

Samples for the coronavirus test will be taken with cotton swabs at the back of the nose and throat. Taking the samples only takes a few seconds, but can cause discomfort and discomfort. Taking a sample from the back of the throat may result in gagging. When the sample is taken at the back of the nose, you may experience a stinging sensation and the eyes may water.

Contacts

Public
Exciva GmbH

Hauptstrasse 25
Heidelberg 69117
DE
Scientific
Exciva GmbH

Hauptstrasse 25
Heidelberg 69117
DE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Elderly (65 years and older)

Inclusion criteria

1. Sex: male or postmenopausal female.
2. Age: 65 to 85 years, inclusive, at screening.
3. BMI :18.0 to 35.0 kg/m2 , inclusive, at screening.
4. Status: healthy subjects.
5. Good physical and mental health based on medical history, physical examination, clinical laboratory, ECG, and vital signs, or the absence of any medical condition which, in the opinion of the Investigator, might prevent compliance with study procedures or completion.
6. Subjects must have a score of >=23 on the Mini-Mental State Exam (MMSE).

Exclusion criteria

1. Evidence of any active or chronic disease or condition that could interfere with, or the treatment of which could interfere with, the conduct of the study, or that would pose an unacceptable risk to the subject in the opinion of the Investigator (following a detailed medical history, physical examination, vital signs [systolic (SBP) and diastolic blood pressure (BP), pulse rate, body temperature], 12lead ECG, and clinical laboratory parameters [hematology,

blood chemistry, and urinalysis]). Minor deviations of laboratory values from the normal range may be accepted, if judged by the Investigator as clinically irrelevant.
2. Previous participation in the current study.
3. Employee of PRA or the Sponsor.
4. History of relevant drug and/or food allergies.
5. History of alcohol abuse or drug addiction (including soft drugs like cannabis products) in the previous 2 years.
6. Positive drug and alcohol screen (opiates, methadone, cocaine, amphetamines [including ecstasy], cannabinoids, barbiturates, benzodiazepines, gamma hydroxybutyric acid [GHB], tricyclic antidepressants, and alcohol) at screening or at the first admission.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-09-2021
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Deramciclane
Generic name:	Deramciclane
Product type:	Medicine
Brand name:	Dextromethorphan

Generic name:	Dextromethorphan

Ethics review

Approved WMO Date:	15-07-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-09-2021
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	EUCTR2021-002665-17-NL
CCMO	NL78397.056.21