Multiple ascending dose study with Memogain.

No registrations found.

Ethical review	Not applicable
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23253

Source
Nationaal Trial Register

Brief title
Memogain MAD

Health condition

Healthy volunteer studie, though drug may ameliorate Alzheimer's Disease symptoms.

-Keywords: Galantamine, Alzheimer, Memogain, NeuroCart

Sponsors and support

Primary sponsor: Neurodyn Life Sciences Inc.
Source(s) of monetary or material Support: Sponsor (Neurodyn Life Sciences Inc.)

Intervention

Outcome measures

Primary outcome

"Tolerability / safety endpoints

• Treatment-emergent (serious) adverse events ((S)AEs) up to 5 pharmacokinetic half-lives

after study drug (i.e. Memogain) discontinuation.

• Treatment-emergent abnormalities in vital signs (blood pressure and pulse rate) until end of study (EOS).

• Treatment-emergent marked ECG abnormalities up to 5 pharmacokinetic half-lives after study drug discontinuation (i.e. Memogain).

• Treatment-emergent marked laboratory abnormalities up to 5 pharmacokinetic half-lives after study drug discontinuation (i.e. Memogain).

• The above 4 endpoints will also be investigated after galantamine administration in cohort 2

• Post-dose nasal examinations.

Pharmacokinetic endpoints

PK model

A population PK model will be developed to describe the pharmacokinetic profile of Memogain and galantamine in plasma. The estimated population values of the model parameters (both fixed and random effects) are used to determine individual empirical Bayes' estimates of the primary pharmacokinetic parameters such as CL/F, V/F and Vss/F, and of derived observable parameters including, but not limited to, Cmax, tmax, AUC-0-, and apparent terminal half-life. Additional PK parameters may be calculated if appropriate.

CSF

To investigate possible differences between concentration of galantamine cleaved from Memogain and concentrations of galantamine following oral administration in the central nervous system, CSF galantamine and Memogain concentrations will be compared within-subject in cohort 2 (Memogain 11mg). 12 subjects that were on active treatment in cohort 2 will be randomized to one of four different CSF sampling time points (i.e. 3 subjects per time point). In total, two CSF samples will be taken per subject (one after Memogain administration on Day 1, and one after galantamine oral administration) to characterise the time-concentration curve for Memogain and galantamine.

PK/PD relationship

The relationship between plasma Memogain and galantamine concentrations and a corresponding selection of relevant pharmacodynamic measurements will be plotted to evaluate the relationship graphically. If the observed pharmacodynamic effects allow it, a suitable PK/PD model will be developed to describe the exposure/concentration-effect relationship.

Pharmacodynamic endpoints

NeuroCart tests, including:

• Adaptive tracking test

• EEG: 21-lead EEG recordings; standard power spectrum analysis

• Event related potentials (ERPs), i.e. P300

• Saccadic and smooth pursuit eye movements

• N-back task (0-back, 1-back and 2-back condition)

• Visual Verbal Learning test

• VAS according to Bond and Lader (alertness, mood, calmness) and nausea"

Secondary outcome

N/A

Study description

Background summary

Recruitment is done in The Netherlands

Study objective

Extension of SAD PK/PD Model, confirmation of SAD PD effects

Study design

"Day 1 t/m 8 for PK

Day 1 and Galantamine day for CSF (cohort 2)"

Intervention

Memogain will be administered intranasally for 7 days b.i.d. (14 doses in total). The 12 subjects from cohort 2 that were on Memogain treatment will be administered galantamine 16 mg once, as well as have lumbar punctures.

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Eligibility criteria

Inclusion criteria

"1. Healthy male or postmenopausal female subjects, aged 65 years and over. Healthy status is defined by the absence of evidence of any active or chronic disease following a detailed medical and surgical history, a complete physical examination including vital signs, 12-lead electrocardiogram (ECG), haematology, blood chemistry, and urinalysis;

2. Body Mass Index (BMI) between 18 kg/m² and 30 kg/m², inclusive, and with a minimum weight of 50 kg;

3. Able to participate and willing to give written informed consent and to comply with the study restrictions;

4. Absence of cognitive impairment evident by a score of 26 or higher on the Mini Mental

State Examination (MMSE);

5. Non-smokers."

Exclusion criteria

"1. Legal incapacity or inability to understand or comply with the requirements of the study;

2. Clinically relevant history of abnormal physical or mental health interfering with the study as determined by medical history taking and physical examinations obtained during the screening visit and/or at the start of the first study day for each period as judged by the investigator;

3. Any disease associated with cognitive impairment, including (but not restricted to) schizophrenia and dementia;

4. Clinically relevant abnormal laboratory results (including hepatic and renal panels, complete blood count, chemistry panel and urinalysis), electrocardiogram (ECG) and vital signs, or physical findings at screening and/or at the start of the first study day for each period (as judged by the investigator). In the case of uncertain or questionable results, tests performed during screening may be repeated before randomization to confirm eligibility or judged to be clinically irrelevant for healthy subjects;

5. Systolic blood pressure (SBP) greater than 145 or less than 90 mm Hg, and diastolic blood pressure (DBP) greater than 90 or less than 50 mm Hg;

6. Notable resting bradycardia (HR < 45 bpm) or tachycardia (HR > 100 bpm) at screening or baseline visit;

7. QtcF >450 or <300 msec at screening or baseline visit;

8. Positive test for Hepatitis B surface antigen (HBsAg), Hepatitis C antibody (HCV Ab), or human immunodeficiency virus antibody (HIV Ab) at screening;

9. Presence or history (within 3 months of screening) of alcohol abuse confirmed by medical history, or daily alcohol consumption exceeding 2 standard drinks per day on average for females or exceeding 3 standard drinks per day on average for males (1 standard drink = 10 grams of alcohol), or a positive breath alcohol test at screening or upon admission to the Clinical Research Unit (CRU), and the inability to refrain from alcohol use from 24 hours before screening, dosing and each scheduled visit until discharge from the clinical research unit (CRU) (alcohol consumption will be prohibited during study confinement);

10. Subject is unable to refrain from alcohol use from 24 hours prior to dosing until discharge from the CRU;

11. Used tobacco and/or nicotine-containing products within 90 days of dosing;

12. Positive urine drug screen (UDS) or alcohol or cotinine test at screening and/or pre-dose;

13. Habitual and heavy consumption of caffeinated beverages (more than 8 cups of coffee or equivalent/day) at screening and/or unable to refrain from use of (methyl) xanthine (e.g. coffee, tea, cola, chocolate) from 24 hours prior to dosing until discharge from the CRU

14. Aspartate transaminase (AST), alanine transaminase (ALT), gamma glutamyl transferase (GGT) or total bilirubin levels >1.5 times the upper limit of normal at screening;

15. Evidence of significant renal insufficiency, indicated by a glomerular filtration rate lower than the lower limit of normal (related to age) at screening;

16. Concomitant use of cholinergic (e.g. varenicline, donepezil, rivastigmine) or anti-cholinergic (e.g. clozapine, olanzapine) medication within 21 days prior to dosing;

17. Concomitant use of inhibitors of CYP2D6 (e.g., kinidine, paroxetine, fluoxetine) or of CYP3A4 (e.g., ketoconazol, ritonavir) within 21 days prior to dosing;

18. Subject is unable to refrain from the use of concomitant medication which, in the opinion of the investigator, interferes with their ability to participate in the trial, from 7 days prior to dosing until the follow-up study visit;

19. Subject has a history of severe allergies, or has had an anaphylactic reaction to prescription or non-prescription drugs or food;

20. Known hypersensitivity to the investigational drug or comparative drug or drugs of the same class, or any of their excipients;

21. History or clinical evidence of any disease and/or existence of any surgical or medical condition which might interfere with the absorption, distribution, metabolism or excretion of the study drugs;

22. Result from nasal examination at screening that, in the investigator or physician’s opinion, could affect drug uptake following intranasal administration;

23. Participation in an investigational drug trial in the 3 months prior to administration of the initial dose of study drug or more than 4 times per year;

24. Donation or loss of blood of more than 500 mL within 3 months (males) or 4 months (females) prior to screening;

25. Any other condition that in the opinion of the investigator would complicate or compromise the study, or the wellbeing of the subject;

26. Unwillingness or inability to comply with the study protocol for any other reason"

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-03-2016
Enrollment:	48
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL5557
NTR-old	NTR5678
Other	: CHDR1543

Study results

Summary results
http://www.alzheimersanddementia.com/article/S1552-5260%2814%2901257-6/abstract