Study to explore the use of potential biomarkers of Gcase enzyme activation in healthy subjects and patients with Parkinson's Disease with and without a mutation in the GBAgene

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON26026

Source
Nationaal Trial Register

Brief title
Biomarker study for GCase activity and enzyme levels

Health condition

Parkinson's Disease
Ziekte van Parkinson

Sponsors and support

Primary sponsor: CHDR
Source(s) of monetary or material Support: CHDR, partial funding by Lysosomal Therapeutics Inc.

Intervention

Outcome measures

Primary outcome

1. GCase activity in whole-blood

2. GCase activity in isolated PBMCs

3. GCase protein in PBMCs

4. GluCer in PBMCs and plasma - Potentially other substrates / products in the same metabolic pathway

Secondary outcome

NA

Study description

Background summary

A biomarker study in healthy adults and patients with PD with and without a GBA mutation. No investigational drug will be administered during this pre-study. Participants will be in-house on Day 1 for five blood draws (the first in fasted state) and fixed breakfast, lunch and dinner. All subjects will return for a short visit on day 5 and 8 for blood donation only, between 9 and 10 AM in fasted state. PD patients will return for two short visits on day 3 and 5. This design will allow assessment of within-day variability, day-to-day variability and inter-individual variability of GCase activity, GCase protein and GluCer or other sphingolipids in healthy subjects and in PD patients with and without a GBA mutation. The patients will be recruited in the Netherlands

Study objective

This phase 0 study will serve to understand the variation in potential pharmacodynamics biomarkers (and methods of analyzing these biomarkers) to be implemented in planned first-in-human single and multiple ascending dose studies with a novel GCase activator

Study design

Medical Screening (1x), Single full day visit with multiple measurements, and 2 return visits on day 5 and 8.

Intervention

NA

Contacts

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Eligibility criteria

Inclusion criteria

Group 1, Inclusion criteria;

1. Signed informed consent prior to any study-mandated procedure.

2. Healthy male and female volunteers, 18 to 65 years of age, inclusive at screening. Healthy status is defined by absence of evidence of any active or chronic disease following a detailed medical history and clinical laboratory parameters (hematology, blood chemistry and urine analysis.

3. Body mass index (BMI) between 18 and 30 kg/m2, inclusive at screening, and with a minimum weight of 50 kg.

4. Has the ability to communicate well with the investigator in the Dutch language and is willing to comply to the study restrictions.

Group 2 & 3, Inclusion criteria;

1. Signed informed consent prior to any study-mandated procedure.

2. Diagnosis of PD at least 6 months prior to screening. The diagnosis requires : the presence of at least 2 of the 4 cardinal clinical manifestations of the disease, tremor, rigidity, bradykinesia, and disturbances of posture or gait.

3. A score of 1-4 on Hoehn & Yahr Scale.

4. Group 2: Confirmed mutation in the glucocerebrosidase (GBA1) gene.

5. Group 3 :Confirmed wild type glucocerebrosidase (GBA1) gene.

6. Mini Mental State Exam score >= 18 and assessed by treating neurologist as mentally competent.

7. Body mass index (BMI) between 18 and 35 kg/m2, inclusive, and with a minimum weight of 50 kg at screening.

8. Has the ability to communicate well with the investigator in the Dutch language and willing to comply to the study restrictions

Exclusion criteria

Group 1, exclusion criteria;

1. Any recent (within 7 days) infectious disease.

2. Positive Hepatitis B surface antigen (HBsAg), Hepatitis B antibodies, Hepatitis C antibody (HCV Ab), or human immunodeficiency virus antibody (HIV Ab) at screening.

3. Use of any medications (prescription or over-the-counter [OTC], within 14 days of screening, or less than 5 half-lives (whichever is longer). Expectations are paracetamol (up to 4g/day) and ibuprofen (up to 1g/day). Other exceptions will only be made if the rationale is clearly documented by the investigator;

4. Participation in an investigational drug or device study within 3 months prior to first sampling.

5. History of abuse of addictive substances (alcohol, illegal substances) or current use of more than 21 units alcohol per week, drug abuse, or regular user of sedatives, hypnotics, tranquilizers, or any other addictive agent;

6. Positive test for drugs of abuse at screening or pre-dose(in case of a positive test result,

the test may be repeated once);

7.Alcohol will not be allowed from at least 24 hours before screening;

8. Smoker of more than 10 cigarettes per day prior to screening or who use tobacco products equivalent to more than 10 cigarettes per day and unable to abstain from smoking whilst staying in the unit;

9. Is demonstrating excess in xanthine consumption (more than eight cups of coffee or equivalent per day;

10. Loss or donation of blood over 500 mL within three months (males) or four months (females) prior to screening or intention to donate blood or blood products during the study;

11. Female subjects who are pregnant, breast-feeding or planning on becoming pregnant during the study;

12. Any known factor, condition, or disease that might interfere with treatment compliance, study conduct or interpretation of the results such as drug or alcohol dependence or psychiatric disease.

Group 2 & 3, Exlcusion criteria;

1. Evidence of any active or chronic disease other than PD that could interfere with, or for which the treatment of might 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 and clinical laboratory parameters (hematology, blood chemistry and urine analysis.

2. Positive Hepatitis B surface antigen (HBsAg), Hepatitis B antibodies, Hepatitis C antibody (HCV Ab), or human immunodeficiency virus antibody (HIB Ab) at screening.

3. History of recent major surgery (within 60 days of screening).

4. Atypical or secondary parkinsonism (in the judgement of the PI).

5. Any recent (within 7 days) infectious disease;

6. Participation in an investigational drug or device study within 3 months prior to first dosing.

7. History of abuse of addictive substances (alcohol, illegal substances) or current use of more than 21 units of alcohol per week, drug abuse, or regular user of sedatives, hypnotics, tranquilizers, or any other additive agent.

8. Positive test for drugs of abuse at screening or pre-dose.

9. Alcohol will not be allowed from at least 24 hours before screening;

10. Smoker of more than 10 cigarettes per day prior to screening or those who use tobacco products equivalent to more than 10 cigarettes per day and unable to abstain from smoking whilst staying at the unit.

11. Is demonstrating excess in xanthine consumption (more than eight cups of coffee or equivalent per day)

12. Loss or donation of blood over 500 mL within three months (males) or four months (females) prior to screening or intention to donate blood or blood products during the study.

13. Any known factor, condition or disease that might interfere with treatment compliance, study conduct or interpretation of the results such as drug or alcohol dependence or psychiatric disease.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	19-03-2017
Enrollment:	24
Type:	Anticipated

Ethics review

Positive opinion

Date:	09-03-2017
Application type:	First submission

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	NL6116
NTR-old	NTR6256
Other	NL60806.056.17 : CHDR1655 /

Study results