• Research study to investigate the safety, tolerability and effects of multiple doses of LTI-291 in patients with Parkinson’s Disease with a GBA1 mutation.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23923

Source
NTR

Brief title
• First-In-Patient study of LTI-291

Health condition

PD patients with a GBA1 mutation , movement disorder

Sponsors and support

Primary sponsor: • Lysosomal Therapeutics, Incorporated
Source(s) of monetary or material Support: • Lysosomal Therapeutics, Incorporated

Intervention

Outcome measures

Primary outcome

• Safety and tolerability endpoints

Secondary outcome

• Functional outcome measures

• Pharmacokinetic endpoints

• Pharmacodynamic endpoints

Study description

Background summary

• Approximately 10% of patients with clinically diagnosed Parkinson’s disease, Lewy Body Dementia, or Diffuse Lewy Body disease have a GBA1 mutation. More recently, it has become clear that even carrying one mutated allele of GBA1 significantly increases the lifetime risk of developing parkinsonism. Existing treatments are symptomatic in nature, and do not modify the underlying disease progression. For patients with GBA-PD, some approaches eg DBS and anti-cholinergic agents may be contra-indicated due to the risk of worsened cognitive decline (Sasagasako et al., 1994; Thaler et al., 2017). Therapies targeting underlying pathogenesis could slow disease progression in this population. Several lines of evidence suggest that activation of GCase enzymatic activity could provide therapeutic benefit to patients carrying a heterozygous mutation in the GBA1 gene. The GCase activator, LTI-291 could be a potential treatment for patients with GBA-PD. All participants will be recruited in the Netherlands

Study objective

• To evaluate the safety and tolerability of three oral dose levels of LTI-291 following 28 days of LTI-291 treatment in patients with Parkinson’s Disease with GBA-PD.

• To characterize the plasma and CSF pharmacokinetics (PK) of LTI-291 following 28 days of LTI-291 treatment in patients with GBA-PD.

• To evaluate the pharmacodynamics of LTI-291 following 28 days of treatment in patients with GBA-PD using biomarker assessments.

Study design

• Screening (up to 30 days before study start); demographics / physical examination / blood sampling / vital signs / ECG / Alcohol breath test / neurocart training

• Day -1 (admission to the clinic) ; Physical / blood sampling / urine collection, ECG / vital signs / CSF sampling / EEG / neurocart

• Day 0 : Vitals / dosing / blood sampling / ECG / discharge

• Day 6 & 13 : vitals / blood sampling / urine collection / ECG and neurocart (only on day 13).

• Day 20: telephone follow up

• Day 26 : admission to the clinic if applicable

• Day 27 : Blood sampling / urine collection / dosing / CSF sample / Vitals / ECG / Alcohol breath test / EEG/ discharge if applicable

• Day 38 (Follow up visit) ; physical examination, blood sampling, vital signs /alcohol breath test

Intervention

• LTI-291 and placebo

Contacts

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Eligibility criteria

Inclusion criteria

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

2. Minimum age of 18 years.

3. Clinical diagnosis of Parkinson’s Disease at least 6 months prior to screening, confirmed by a neurologist.

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

5. Mutation(s) in glucocerebrosidase GBA1 gene.

6. Mini Mental State Exam score >/= 18 and assessed by the investigator or qualified designee as able to provide informed consent.

7. Body mass index (BMI) between 18 and 35 kg/m2, inclusive, and with a minimum weight of 45 kg at screening.

8. All females must be at least 2 years post-menopausal or surgically sterile or practice highly effective contraception until at least 90 days after their last dose of study treatment.

9. All males must practice effective contraception and abstain from sperm donation during the study and be willing and able to continue contraception for at least 90 days after their last dose of study treatment.

10. Has the ability to communicate with the investigator and is willing to comply with the study restrictions.

Exclusion criteria

1. Any active or chronic disease or condition other than PD that could interfere with, or for which the treatment 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 medical history review, physical examination, vital signs (supine systolic and diastolic blood pressure, pulse rate, body temperature), 12-lead electrocardiogram (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 to have no clinical relevance.

2. History of recent major surgery (within 60 days of screening) that could interfere with, or for which the treatment might interfere with, the conduct of the study, or that would pose an unacceptable risk to the subject in the opinion of the investigator.

3. Atypical or secondary parkinsonism by medical history or in the opinion of the investigator. Atypical parkinsonism includes, but not limited to a diagnoses of progressive supranuclear palsy, corticobasal syndrome and multiple system atrophy. Secondary parkinsonism includes drug-induced, post-infectious, post-traumatic and vascular parkinsonism.

4. Patients that experience Freezing Of Gait (FOG) in the on-state of L-dopa treatment (paradoxical response), which might interfere with the conduct of the study, or that would pose an unacceptable risk to the subject in the opinion of the investigator.

5. Current (within last 30 days prior to start of clinical phase) use of a strong CYP3A4 modulator. Reference Appendix B for a list of prohibited CYP3A4 modulators.

6. Current use of any drug known to significantly inhibit blood coagulation in the opinion of the investigator.

7. Vaccination within 7 days prior to start of dosing.

8. Any contra-indication for undergoing a lumbar puncture procedure (e.g. anatomical variations or local skin infection).

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

10. Participation in an investigational drug or therapeutic device study within 3 months prior to first dosing, or within 6 months for a biologic investigational product.

11. Recent history (last 6 months) of abuse of addictive substances (alcohol, illegal substances) or current use of more than 21 units of alcohol per week, drug abuse, or regular recreational user of sedatives, hypnotics, tranquillizers, or any other addictive agent.

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

13. Women currently pregnant or breastfeeding.

14. 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.

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-12-2017
Enrollment:	40
Type:	Actual

Ethics review

Positive opinion

Date:	17-01-2018
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	NL6574

Register	ID
NTR-old	NTR6960
Other	NL62049.056.17 / 2017-004086-27 / LTI-291-003 : CHDR1710

Study results

Summary results
NA