Observational Assessment of Clinical and Genetic Risk Factors Associated with GBA1-Associated Parkinson's Disease Clinical Progression: A genetic Analysis and Retrospective Study

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Movement disorders (incl parkinsonism)
Study type	Observational non invasive

Summary

ID

NL-OMON46323

Source
ToetsingOnline

Brief title
Clinical and Genetic Risk in GBA-PD

Condition

- Movement disorders (incl parkinsonism)

Synonym
GBA-Parkinson's disease

Research involving
Human

Sponsors and support

Primary sponsor: Lysosomal Therapeutics Incorperated
Source(s) of monetary or material Support: Lysosomal Therapeutics;Incorporated

Intervention

Keyword: GBA 1 gene, Genetic Risk Score, Parkinson's Disease

Outcome measures

Primary outcome

Based on multiple parameters, the following compound measurements are

constructed:

- Parkinson*s disease * Progression Rate Inventory (PD-PRI)

- GBA1 genotype and PD associated SNPs

- Parkinson*s Risk Score (PRS)

- Rate of disease progression as rated by a clinical expert: Slow,

Intermediate, Fast

The endpoints are the analyses of the associations between:

* genetic factors and phenotypic factors

* genetic factors and the rate of disease progression as rated by a Movement

Disorder Neurologist

* genetic factors and a data-driven algorithm based on phenotypic

characteristics

Secondary outcome

N.A.

Study description

Background summary

The current protocol is a follow-up on the previous study CHDR1707 (Toetsing online number: NL61137.056.17), titled *Genetic screening in Parkinson*s Disease in order to identify patients who can participate in clinical trials with new targeted therapies.* In this previous study, Parkinson*s patients throughout the Netherlands were genetically screened for presence of mutations in the GBA1 gene and LRRK2 gene. In approximately 15% of all screened patients, a mutation was found in the GBA1 gene (Figure 1). The current protocol aims to further characterize this subgroup of patients with a GBA1 mutation, based on phenotype, as assessed by medical history, and on genotype, as assessed by Parkinson*s disease related Single Nucleotide Polymorphism (SNP) analysis. The goal of this study is to exploratively investigate whether clinical and genetic factors may contribute to the rate of clinical progression in patients with Parkinson*s disease associated with a GBA1 mutation in the gene encoding GCase (GBA-PD).

Study objective

* To determine the relationship between phenotypic and genetic characteristics of GBA-PD patients. Phenotypic characteristics will be obtained by patient dossier review. Genetic characteristics comprise of the GBA1 gene and a panel of SNPs, previously associated with risk or progression of idiopathic Parkinson*s disease.
* To determine the correlation between genetic characteristics (as described above) and the estimated disease progression rating (Fast, Intermediate, Slow) by a Movement Disorders Neurologist, based on retrospective phenotypic characteristics (as described above).
o Inter-rater correlation between Movement Disorders Neurologists will be determined.
* To determine the correlation between genetic characteristics (as described above) and a data-driven algorithm based on phenotypic characteristics (as described above).

Study design

This will be an exploratory retrospective medical history review and genetic analysis study in previously identified GBA-PD patients from a number of clinics in the Netherlands.
GBA-PD patients from the following 5 clinics will be enrolled in the present study: Amsterdam UMC location AMC, LUMC, St. Antonius ziekenhuis, Spaarne Gasthuis and UMCG. Patients will provide informed consent for clinical history review and further genetic analyses (in addition to the already known GBA1

mutation).

Study burden and risks

The burden/inconvenience for the patient is minimal and the information we obtain can be very valuable for further research.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

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 Movement Disorder*s Neurologist.
4. Mutation(s) in the glucocerebrosidase GBA1 gene. Reference Appendix A for a list of GBA1 mutations.

Exclusion criteria

N.A.

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-06-2019
Enrollment:	350
Type:	Actual

Ethics review

Approved WMO

Date:	10-10-2018
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

ID: 28601
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL67297.056.18