

# Genetic screening for GBA1 in Parkinson's disease patients

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<b>Registration date</b> 08/11/2023	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 08/11/2023	<b>Condition category</b> Nervous System Diseases	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background of the study

Parkinson's disease (PD) is a common neurodegenerative disease, present in 1-2% of individuals aged  $\geq 65$  years. The most common genetic risk factor for PD is a heterozygous mutation in the GBA1 gene. In a previous study, it was demonstrated that 15% of PD patients in the Netherlands have a mutation in the GBA1 gene. GBA1 encodes for beta-glucocerebrosidase (GCase), a lysosomal enzyme that is responsible for the hydrolysis of glucosylceramide to ceramide and glucose. A mutation in GBA1 causes lysosomal dysfunction and it is hypothesized that this eventually leads to the accumulation of alpha-synuclein which is the hallmark of PD. PD patients with a mutation in the GBA1 gene exhibit an earlier onset of disease and have an increased risk of cognitive decline but can otherwise not be differentiated from idiopathic PD patients based on phenotype. For an upcoming Phase Ib trial investigating a potential disease-modifying therapy in the form of a GCase activator (VQ101) developed by Vanqua Bio, this study aims to identify potential study participants with a mutation in the GBA1 gene. To identify this group of PD patients, a large screening study will be conducted.

### Who can participate?

PD patients aged between 40 and 80 years old

### What does the study involve?

The genetic screening for mutations in the GBA1 gene will be performed through saliva sampling. Samples will be taken by PD patients at home with a saliva sampling kit that will be sent to them via mail. Participation in the genetic screening study will consist of the following sequential steps:

1. Information phase: Awareness will be raised in collaboration with the treating neurologist and/or media advertisement. Potential participants can contact CHDR and be provided with verbal and written information on the study design and requirements.
2. Consent phase: If the patient is interested in participating, written informed consent will be obtained
3. Sampling phase: Following informed consent, patients will provide a saliva sample through a saliva sampling kit that is sent to the patient to use at home
4. Sequencing phase: The saliva kit will be sent to CHDR and thereafter to GenomeScan for sequencing

5. Counselling phase: Patients will be informed on the outcome of the sequencing in writing and offered counselling as deemed appropriate by the investigator

What are the possible benefits and risks of participating?

This research serves to obtain PD patients with a mutation in their GBA1 gene; the risk and burden for the subject are minimal and by identifying these patients, further research can be done with a novel potentially disease-modifying drug for PD patients with a GBA1 mutation.

This study requires a saliva sampling. The procedure for this is with a saliva sampling kit which can be performed at home. The kits can be returned by mail. The burden for patients is minimal and there are no risks associated with the procedure.

Where is the study run from?

The Centre for Human Drug Research (CHDR) (Netherlands)

When is the study starting and how long is it expected to run for?

April 2023 to November 2024

Who is funding the study?

Vanqua Bio Inc. (USA)

Who is the main contact?

E. Thijssen, [clintrials@chdr.nl](mailto:clintrials@chdr.nl) (Netherlands)

## Contact information

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Principal investigator

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## Additional identifiers

**Clinical Trials Information System (CTIS)**

Nil known

**ClinicalTrials.gov (NCT)**

Nil known

**Protocol serial number**

CHDR2327/VQ-002

## Study information

**Scientific Title**

Genetic screening in Parkinson's disease patients to identify GBA1 mutation carriers for future clinical trials

**Study objectives**

For an upcoming Phase 1b trial investigating a potential disease-modifying therapy in the form of a GCase activator (VQ101) developed by Vanqua Bio, this study aims to identify potential study participants with a mutation in the GBA1 gene. To identify this group of PD patients, a large screening study will be conducted.

**Ethics approval required**

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**Ethics approval(s)**

approved 02/11/2023, Stichting BEBO (Dr. Nassaulaan 10, Assen, 9401 HK, Netherlands; +31 592 405 871; info@stbebo.nl), ref: NL85000.056.23

**Study design**

Genetic screening study

**Primary study design**

Observational

**Study type(s)**

Screening

**Health condition(s) or problem(s) studied**

Parkinson's disease, Parkinsonism

**Interventions**

Parkinson's disease (PD) is a common neurodegenerative disease, present in 1-2% of individuals aged  $\geq 65$  years. The most common genetic risk factor for PD is a heterozygous mutation in the GBA1 gene. In a previous study, it was demonstrated that 15% of PD patients in the Netherlands have a mutation in the GBA1 gene. GBA1 encodes for beta glucocerebrosidase (GCase), a lysosomal enzyme that is responsible for the hydrolysis of glucosylceramide to ceramide and glucose. A mutation in GBA1 causes lysosomal dysfunction and it is hypothesized that this eventually leads to the accumulation of alpha-synuclein which is the hallmark of PD. PD patients with a mutation in the GBA1 gene exhibit an earlier onset of disease and have an increased risk of cognitive decline but can otherwise not be differentiated from idiopathic PD patients based on phenotype. This study aims to genetically screen patients for mutations in the GBA1 gene.

The genetic screening for mutations in the GBA1 gene will be performed through saliva sampling. Samples will be taken by PD patients at home with a saliva sampling kit that will be sent to them via mail by CHDR staff. Awareness for the study will be raised in collaboration with the treating neurologists of the PD patients and through advertisement by CHDR via (social) media. If a patient contacts the CHDR and wishes to participate, an informed consent document will be provided via mail. Once a completed ICF is obtained by CHDR, the saliva kit will be sent by CHDR to the patient. The saliva sample will be labelled with a subject-specific code to ensure sample pseudonymization. Only CHDR has the code to link the saliva sample to the patient. Saliva samples will thereafter be sent to the laboratory of GenomeScan for next-generation sequencing using the Illumina NovaSeq sequencer, generating  $>400,000$  150 bp paired-end reads. All patients will be informed of the result of the sequencing and offered further counselling if applicable. This counselling can be done either via CHDR or via the treating neurologist at the local hospital if preferred.

**Intervention Type**

Other

**Primary outcome(s)**

Sequence of the full GBA1 gene, classified as wildtype or mutated, with specifications of the mutation measured using next-generation sequencing at one timepoint

**Key secondary outcome(s)**

There are no secondary outcome measures

**Completion date**

30/11/2024

**Eligibility****Key inclusion criteria**

1. Age 40-80
2. All participants must understand and provide written informed consent prior to any study-specific procedures
3. Able to speak, read, and understand study procedures in Dutch sufficiently to allow completion of all study assessments
4. Confirmed clinical diagnosis of Parkinson's disease by a neurologist within the last 5 years, based on presence of bradykinesia and either resting tremor and/or muscular rigidity in at least one limb
5. Willing to be contacted regarding potential participation in future interventional clinical trials

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Mixed

**Lower age limit**

40 years

**Upper age limit**

80 years

**Sex**

All

**Key exclusion criteria**

1. History of a significant medical or psychiatric comorbidity that would preclude the subject's participation in an interventional clinical trial
2. Known GBA-1 mutation for Parkinson's disease

**Date of first enrolment**

08/11/2023

**Date of final enrolment**

30/09/2024

**Locations**

## Countries of recruitment

Netherlands

## Study participating centre

The Centre for Human Drug Research

Zernikedreef 8

Leiden

Netherlands

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## Sponsor information

### Organisation

Vanqua Bio Inc.

## Funder(s)

### Funder type

Industry

### Funder Name

Vanqua Bio Inc.

## Results and Publications

### Individual participant data (IPD) sharing plan

The data-sharing plans for the current study are unknown and will be made available at a later date.

### IPD sharing plan summary

Data sharing statement to be made available at a later date

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes