ISRCTN99451262 https://doi.org/10.1186/ISRCTN99451262

Genetic screening for GBA1 in Parkinson's disease patients

Submission date
31/08/2023

Recruitment status
No longer recruiting

Registration date
08/11/2023

Overall study status
Completed

Last Edited
08/11/2023

Condition category
Nervous System Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] 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 ≥ 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 (Netherlands)

Contact information

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Additional identifiers

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
Ethics approval required

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

Primary study design
Observational

Study design
Genetic screening study

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 ≥ 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
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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