A multi-center, non-randomized study to characterize biomarkers in cerebrospinal fluid (CSF) of patients with infantile-onset (IOPD) or late-onset Pompe disease (LOPD)

Published: 25-05-2023
Last updated: 07-04-2024

To evaluate Hex4 concentrations in CSF from patients with infantile-onset (IOPD) and late-onset (LOPD) Pompe disease

Ethical review	Not approved
Status	Will not start
Health condition type	Metabolic and nutritional disorders congenital
Study type	Interventional

Summary

ID

NL-OMON56183

Source
ToetsingOnline

Brief title
ASY17795

Condition

- Metabolic and nutritional disorders congenital

Synonym
acid alpha glucosidase deficiency, Pompe Disease

Research involving
Human

Sponsors and support

Primary sponsor: Sanofi BV
Source(s) of monetary or material Support: Sanofi

Intervention

Keyword: Biomarker, CSF, Pompe

Outcome measures

Primary outcome

Primary objective:

To evaluate Hex4 concentrations in CSF from patients with infantile-onset

(IOPD) and late-onset (LOPD) Pompe disease

Endpoint:

Concentration of Hex4 in CSF of patients with IOPD and LOPD

Secondary outcome

Secondary objectives:

-To evaluate Hex4 concentrations in plasma and urine of patients with IOPD and

LOPD

-To evaluate inflammatory biomarkers, including NfL, in CSF, and concomitantly

in plasma and/or serum, of patients with IOPD and LOPD

Endpoints:

-Concentration of Hex4 in plasma and of creatinine normalized Hex4 in urine,

concomitantly drawn at the time of CSF collection, of patients with IOPD and

LOPD

-Concentration of biomarkers, including NfL, in CSF, plasma and/or serum from

patients with IOPD and LOPD

Study description

Background summary

Pompe disease is a rare neuromuscular disorder caused by a genetic deficiency of acid alpha-glucosidase (GAA) that results in lysosomal accumulation of glycogen and subsequent neuromuscular pathology (1). Current standard of care enzyme replacement therapies (ERT) do
not treat central nervous system (CNS) involvement (2, 3, 4, 5). An understanding of CNS pathogenesis and disease progression is critical in these patients. Hexose tetrasaccharide (Hex4), a biomarker reflective of glycogen accumulation, used clinically for diagnosis (6, 7), is potentially
useful as a biomarker of CNS disease. Although CSF Hex4 is elevated in an animal model of Pompe disease (JCR Pharmaceuticals, World Symposium 2021; unpublished Sponsor data), no data are available regarding this biomarker in CSF of patients with Pompe disease. The primary
goal of this study is to understand whether CSF Hex4 and other inflammatory biomarkers, including neurofilament light chain (NfL), are elevated in patients with Pompe disease and could be further evaluated in clinical trials to monitor CNS glycogen accumulation.

Study objective

To evaluate Hex4 concentrations in CSF from patients with infantile-onset (IOPD) and late-onset (LOPD) Pompe disease

Study design

Multi-center, non-randomized

Intervention

not applicable

Study burden and risks

Patients will perform 2 visits of a maximum duration of 2 hours per visit: a screening visit during which the informed consent will be discussed and the second visit to undergo the planned procedure including study procedures. The

procedures for this study are a single venipuncture, onetime urine collection, and a single lumbar puncture. Patients with Pompe disease who have to undergo a procedure for which they are sedated as part of their standard of care or treatment will be asked to participate in the study. In this way there is no extra sedation moments for the patients. IOPD patients annually undergo an MRI under sedation (these young patients otherwise cannot lie still for long enough), LOPD patients occasionally have a malfunctioning venous port, which is replaced under sedation.

Risks related to lumbar punctures and venipunctures (the actual study procedures):

Lumbar puncture: there may be some local pain and the puncture may cause bruising (bruising) or bleeding. There may be post-punctual headache, infection (meningitis or epidural abscess), spinal hematoma, nerve root damage, or cerebral hernia.

Venipuncture: this may be a little painful and the puncture may cause a bruise.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)
Babies and toddlers (28 days-23 months)
Newborns

Inclusion criteria

I 01. Participants who have a confirmed diagnosis of LOPD and clinical signs or symptoms OR
participants who have a confirmed diagnosis of IOPD.
I 02. Capable of giving signed informed consent as described in Appendix 1 (Section 10.1) of
the protocol which includes compliance with the requirements and restrictions listed in the
informed consent form (ICF) and in this protocol; OR If participant is <18 years old,
parent(s) or legally authorized representative(s) (LAR) must be capable of giving signed
informed consent as described in Appendix 1 (Section 10.1) which includes compliance
with the requirements and restrictions listed in the ICF and in this protocol.

Exclusion criteria

E 01. Chronic illness, except for LOPD, IOPD, or directly resulting from Pompe disease, that, at
the discretion of the Investigator, could have an impact on Hex4 and inflammatory markers in the CSF.
E 02. Any acute illness that, at the discretion of the Investigator, could have an impact on Hex4
and inflammatory markers in the CSF.
E 03. High risk of complications from lumbar puncture or potentially associated procedural
sedation, as judged by the Investigator.
E 04. Concurrent treatment with any experimental drug or experimental vaccine.
E 05. Participation in another clinical trial with any investigational drug within 30 days or 5 half-lives, whichever is greater, prior to study start (Day 1).

E 06. Previous participation in any clinical trial involving gene therapy.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	3
Type:	Anticipated

Ethics review

Not approved

Date:	25-05-2023
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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
CCMO	NL83999.000.23