Quantifying disease progression in LBSL

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Objective: The primary objective of this proposal is to develop new sensitive and quantitative outcome measures for clinical trials in LBSL. The secondary objective is to identify biomarkers to stratify patients based on disease progression rate.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Neurological disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON54947

Source
ToetsingOnline

Brief title
Disease progression in LBSL

Condition

- Neurological disorders congenital
- Spinal cord and nerve root disorders

Synonym
Leucoencephalopathy with brainstem and spinal cord involvement and lactate elevation; DARS2

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: NWO Vidi,Unrestricted research grant

Intervention

Keyword: LBSL, Leukodystrophy, myelopathy

Outcome measures

Primary outcome

Progression of disease on all parameters.

Secondary outcome

1) to validate the new outcome measures (i.e. is the biomarker predictive) in

this cohort.

2) to establish if pre-symptomatic patients, and severely affected patients

also show progression on the outcome measures under investigation and if that

means these patients will become eligible for clinical studies.

3) acquire normative data on new potential outcome measures in a cohort of

healthy controls.

Study description

Background summary

Patients with Leukencephalopathy with Brain Stem involvement and Lactate elevation (LBSL) develop cerebral white matter abnormalities and a myelopathy with predominantly degeneration of the pyramidal tracts and dorsal columns. Although early onset disease (even neonatal) is possible, most patients present in adulthood with a slowly progressive gait disorder and incontinence. Currently, there is no disease-modifying treatment and options to quantify myelopathy are limited. Quantifying disease severity is of the utmost importance in studies to determine efficacy of new treatments. Recent studies in other neurodegenerative disorders showed that optical coherence tomography (OCT) and quantitative MRI (DTI) can distinguish between symptomatic and asymptomatic patients and worsen with disease progression. These techniques as well as body sway analysis and gait analysis are potential useful outcome measures of the severity of the myelopathy in LBSL and other neurodegenerative diseases with symptoms and signs of myelopathy and will allow for efficient

clinical trial design.

Study objective

Objective: The primary objective of this proposal is to develop new sensitive and quantitative outcome measures for clinical trials in LBSL. The secondary objective is to identify biomarkers to stratify patients based on disease progression rate.

Study design

This study is a 5-year prospective cohort study, with visits to the hospital every 12 months. For the body sway analysis, gait analysis and MRI studies matched controls will also be evaluated.

Study burden and risks

Currently, patients with LBSL visit the hospital once a year for a neurological examination, and MRI scan of the brain (frequency depends on physician). The frequency of these hospital visits will not change, but additional data will be collected. There is no treatment intervention and all study procedures are low-risk.
Healthy controls will only participate in the functional and quantitative testing (three times in total: at baseline and, 3- and 5-year follow-up) and MRI scans (two times in total: at baseline and 5-year follow-p), Multiple MRI scans in healthy controls are necessary for longitudinal comparison with patients and in order to see whether quantitative MRI measures change over time in the healthy control group. three times in total: at baseline and , 3-, and 5-year follow-up. Each functional measurement will take about 15 minutes. The MRI-scan will take about 60 minutes. Participation has no risks.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- Age > 16 years
- Definite diagnosis of LBSL confirmed by DARS2 mutation analysis.
- Able to understand Dutch or English and provide informed consent.
- No contra-indications for MRI of brain and spinal cord.

Subjects eligible to participate as healthy controls must meet all of the following criteria:
- Willing to visit the hospital
- 16 years or older
- Provision of written informed consent to participate in the study obtained from the participant
For the MRI controls
- No contra-indications for MRI of brain and spinal cord.

Exclusion criteria

Pediatric patients
Unable to provide informed conset

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-10-2021
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO

Date:	26-04-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL74024.018.21