Phenotyping and Exploring biomarkers in Asymptomatic Relatives of aLS variants

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

Summary

ID

NL-OMON53346

Source
ToetsingOnline

Brief title
PEARLS

Condition

- Neuromuscular disorders

Synonym
Amyotrophic lateral sclerosis, lou gehrig disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Vidi beurs,Utrecht-Leuven collaboration grant van de Commissie Internationalisering

Intervention

Keyword: Amyotrophic Lateral Sclerosis, Biomarkers, Presymptomatic

Outcome measures

Primary outcome

Multimodal biomarkers are being researched in order to identify early signs of disease onset in asymptomatic carriers of ALS-related mutations. To validate the efficacy of potential biomarkers they will be compared between ALS/PMA/PLS patients, asymptomatic carriers and non-carriers.

Difference in investigational biomarkers between non-carrier, presymptomaticasymptomatic carrier, phenoconverter and ALS patient levels, and genotype-related differences:

- Liquid biomarkers (based on CSF and urine): e.g. Neurofilament light (NfL), Chitinases, Monocyte chemoattractant protein-1 (MCP-1), p75 extracellular domain (p75ECD) Neurotrophin receptor.
- Fasciculation incidence, muscle wasting
- Eye movement abnormalities
- Cognitive changes in VR tasks.
- Vital capacity reduction.

Secondary outcome

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Study description

Background summary

Genotype-specific therapies for Amyotrophic Lateral Sclerosis (ALS) are approaching quick, with Tofersen for SOD1-ALS already being in use. However, there is often a delay from symptom onset till diagnosis of one year and these compounds take up to another year before therapeutic effect becomes visible, while survival from symptom onset is in certain genotypes only 2 years (e.g. FUS-ALS). As such, early detection of disease onset, is crucial in order to reduce invalidity and mortality.

Study objective

The primary objective is to identify early signs of disease onset in asymptomatic carriers of ALS-related mutations. This will allow them to initiate treatment or partake in clinical trials in an early stage of morbidity.

Secondary Objectives are:
- To test the validity and utility of promising biomarkers that predict the onset of the disease process, that carry prognostic value and/or facilitate the diagnosis.
- To map the natural course of disease from asymptomatic stage till further in the disease.
- To identify phenotypical differences related to carriership.
The biobank objectives is to collect urine and CSF of 200 individuals of aforementioned population in a recurrent longitudinal manner.

Study design

Combined multimodal longitudinal cohort study (WMO) and Biobank

Study burden and risks

The benefit for the pre-symptomatic participants is that they are regularly seen by a physician and symptoms or (biochemical) signs of disease onset are detected early in the disease course. This allows these so called phenoconverters to either receive treatment early on or take part in trials with investigational medical compounds.
Visits are scheduled to take place once a year, whereby most participants are expected to also take part in other ALS-related studies where they are seen by a physician. If not, then according to participant preference, more frequent visits aretwo visits per year are possible.
Ultrasound is a procedure that generally does not cause discomfort. Lumbar punction is a safe procedure to collect CSF, although for some patients an unpleasant experience, hence this is also optional and will only be performed once a year. All genotype-specific treatments for ALS, both proven and under

investigation, are being dosed intrathecal, i.e. by performing lumbar punction. Both in clinic and in clinical trials our experience is that patients cope with this procedure well. Eye movement tracking happens with a device placed on the head of the subject for a couple of minutes and causes no discomfort. VR-tasks are in general being regarded quite entertaining by subjects.

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

- Age >= 18 year
- Being either an ALS/PLS/PSMA patient carrying a pathogenic mutation OR being a relative of such a patient.
- Participant in the NMZ Biobank

Exclusion criteria

none

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	25-07-2023
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO Date:	31-05-2023
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	16-10-2024
Application type:	Amendment
Review commission:	METC NedMec

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	NL83592.041.23