A 5-year Natural History Study in LAMA2-related muscular dystrophy and SELENON-related myopathy: the extended LAST STRONG Study

Published: 26-09-2023
Last updated: 12-10-2024

With the extended LAST STRONG Study, we aim to (1) collect 3-year and 5-year natural history data, (2) implement the natural history data collection into clinical care and international guidelines (reach trial readiness), and (3) do in-depth...

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

Summary

ID

NL-OMON53276

Source
ToetsingOnline

Brief title
extended LAST STRONG Study

Condition

- Muscle disorders

Synonym
LAMA2 and SELENON

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: Prinses Beatrix Spierfonds;Stichting Voor Sara en cure CMD

Intervention

Keyword: LAMA2-related muscular dystrophy, natural history study, outcome measures, SELENON-related myopathy

Outcome measures

Primary outcome

The primary outcome of this study will be the MFM-20/32. Further, a wide

variety of tests will be performed to get a full impression of the patient*s

abilities and disabilities (e.g. neurological examination and functional

measurements, questionnaires, imaging, pulmonary assessment, accelerometry).

The tests that the patient undergoes depend on the age/abilities/wishes.

Secondary outcome

The results of all other tests than MFM-20/32

Study description

Background summary

Selenoprotein N-related congenital myopathy (SELENON-RM) is a rare congenital myopathy with an estimated prevalence of 0.5 in 1.000.000. Key characteristics include slowly progressive axial muscle weakness, early-onset rigidity of the spine, scoliosis and respiratory insufficiency. Delayed motor development is the most common presenting sign. Laminin α2-related muscular dystrophy (LAMA2-MD) is a rare congenital muscular dystrophy with similar key features and an estimated prevalence of 4 in 500.000. It has a disease spectrum ranging from a severe, early-onset congenital muscular dystrophy type 1A ((MDC1A); complete merosine deficiency) to a mild, childhood- or adult-onset limb-girdle type muscular dystrophy (partial merosine deficiency). In addition, patients may suffer from epileptic seizures and may show characteristic diffuse brain white matter lesions on magnetic resonance imaging (MRI). The clinical diagnosis of LAMA2-MD and SELENON-RM is confirmed by recessive pathogenic loss-of-function variants in the LAMA2 or SELENON gene, respectively.

Currently, no curative treatment options exist for neither SELENON-RM nor LAMA2-MD. To determine the effectivity of possible treatment options in clinical trials, it is essential to identify and characterize patients clinically and genetically, and to select clinical and functional outcome measures that correlate with muscle function and that are sensitive to change over time. Up to now, several large clinical studies have been performed. These studies had major limitations, including a retrospective design, the absence of standardized functional measurements and convenient muscle visualizing techniques, and a limited age range.

The LAST STRONG Study, a natural history study to select outcome measures and reach trial readiness, was initiated in 202010. Consensus on the outcome measures will be reached after a key-opinion (pediatric and adult) leader workshop (KOL), which took place in March 2023 at the international LAMA2 conference in Barcelona. Currently, baseline data is analyzed, including decreased bone quality resulting in fragility fractures and impaired pulmonary function starting at young age. In both SELENON-RM and LAMA2-MD, axial and proximal muscle weakness was most pronounced and muscle ultrasound revealed that echogenicity was symmetrically increased. Further, physical activity as measured through accelerometry showed strong correlations with the MFM-20/32 score for both SELENON-RM and LAMA2-MD.

In conclusion, a long-term prospective natural history study in an unselected patient cohort including clinical and functional outcome measures is lacking in both SELENON-RM and LAMA2-MD. Due to the promising ongoing preclinical trials, there is a high need to obtain natural history data in order to reach trial readiness.

Study objective

With the extended LAST STRONG Study, we aim to (1) collect 3-year and 5-year natural history data, (2) implement the natural history data collection into clinical care and international guidelines (reach trial readiness), and (3) do in-depth analysis of the striking results of the LAST STRONG study and collection of serum (muscle biomarkers) and urine. This study will enable a smooth transition towards implementation into clinical care and clinical trials starting within 5 years.

Study design

The extended LAST STRONG Study will be a prospective, single-center, observational cohort study with repeated measurements performed at the Department of Neurology and Pediatric Neurology within the neuromuscular center of the Radboud university medical center, the Netherlands. SELENON-RM and LAMA2-MD patients are invited to visit our hospital two times (three years (visit 5) and five years (visit 6) after the first visit in the LAST STRONG

Study (figure 1)).

Study burden and risks

The aim of this study is to investigate the natural history of SELENON-RM and LAMA2-MD patients to prepare them for clinical trials that are in preparation. Since there are few patients with these conditions, we will ask both children and adults to participate. This study is a preparation for clinical trials in these conditions, may facilitate the proper conduction of these clinical trials and may help to implement natural history data collection into clinical care and international guidelines. The conduction of so many tests is without any doubt burdensome for patients. Therefore, we reduced the number of tests to-our-opinion the absolute minimum based on the first results of the 1.5 year natural history study (LAST STRONG Study) and after the KOL in March 2023. All tests that will be applied during this study, are considered to be of low risk for the participants.

Contacts

Public
Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 10
Nijmegen 6525 GA
NL
Scientific
Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 10
Nijmegen 6525 GA
NL

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)

Inclusion criteria

- 0-100 years of age.
- Willing and able to complete (part of) the measurement protocol at the Radboudumc. If patients do not wish or are not able to visit our neuromuscular center, they are offered to participate in our study through home visits.
- Genetic confirmation of LAMA2-MD or SELENON-RM by two recessive (likely) pathologic mutations in the LAMA2 or SELENON gene, respectively.
- Typical clinical and histological characteristics combined with genetic confirmation in a first degree relative.

Exclusion criteria

- Insufficient understanding of the Dutch language.
- Unwillingness of the patient or his/her legal representatives to provide written informed consent (IC).

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	06-10-2023

Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	26-09-2023
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL84381.091.23