FSHD Longitudinal Biomarker Preparatory Study

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Musculoskeletal and connective tissue disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON46095

Source
ToetsingOnline

Brief title
FSHD LoBiPS

Condition

- Musculoskeletal and connective tissue disorders congenital
- Musculoskeletal and connective tissue disorders congenital

Synonym
FSHD; spierziekte

Research involving
Human

Sponsors and support

Primary sponsor: Fulcrum Therapeutics
Source(s) of monetary or material Support: Fulcrum therapeutics

Intervention

Keyword: Biomarker, DUX4, FSHD, Muscle

Outcome measures

Primary outcome

The primary endpoint is the measurement of DUX4-activation under natural history conditions using a panel of DUX4-regulated gene transcripts in skeletal muscle needle biopsies from FSHD patients obtained 4-8 weeks apart (DUX4 activation Endpoint).

Secondary outcome

The secondary endpoint is the measurement of skeletal muscle tissue replacement by fat in FSHD patients under natural history conditions using whole body MRI obtained 4-12 weeks apart (MRI fat fraction Endpoint).

Study description

Background summary

Fulcrum, in collaboration with leading academic investigators, will perform a biomarker preparatory study to further optimize the methodology and procedures for key molecular (Evidence of DUX4 activation) and imaging (skeletal muscle tissue replacement by fat) efficacy biomarker endpoints in anticipation of a planned proof of concept study of FTX-1821 in FSHD.
The proposed key efficacy biomarkers for this preparatory study are the following:
(1) Evidence of DUX4 activation: A molecular panel of DUX4-regulated gene transcripts to measure DUX4 activation in skeletal muscle needle biopsies from patients with FSHD.
(2) Skeletal Muscle Tissue Replacement by Fat: A whole-body MRI imaging protocol and analysis algorithms to measure replacement of skeletal muscle tissue by fat in FSHD.

Study objective

The primary objective of this study is the further evaluation and optimization of skeletal muscle tissue and MRI biomarkers for a planned POC study of FTX-1821 in FSHD. Therefore, this study is not a drug trial but rather a preparatory biomarker study to enable a planned therapeutic trial.

Study design

This will be a prospective, longitudinal, observational, multicenter study

Study burden and risks

Participants will be asked for 4 visits to the outpatient clinic at the department of neurology. Their medical history will be taken, they will undergo clinical examination and they will fill out questionnaires. Blood samples will be collected at each visit.
MRI scanning and muscle biopsies will be performed at two of the visits. Risks to subjects may be physical (e.g., bruising during muscle strength testing). There is a small risk of bruising from blood draws. Muscle biopsy is an invasive procedure that can be painful, and can lead to complications such as hematoma or infections. All procedures will be performed according to standard accepted techniques to minimize risk exposure for subjects. We classify the risk of this study as negligible.

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

(1) Age 18-60 years old.
(2) Ability to provide informed consent.
(3) Confirmed diagnosis of FSHD1 with 1-7 repeats via assessment of the size of the D4Z4 array on chromosome 4. Enrollment may be controlled to ensure that patients with both lower (1-3) and higher (4-7) repeat numbers are included.
(4) Clinical Severity Score between 2 and 4 on Ricci*s scale (scale range is from 0 to 5).
(5) Commitment to complete the two visits for skeletal muscle needle biopsy and whole-body MRI.
(6) Able to complete the RWS, TUG and FSHD PRO at the screening visit.
(7) Presence of STIR positive signal in at least one leg skeletal muscle eligible for needle biopsy, at screening MRI.

Exclusion criteria

(1) Any condition that in the opinion of the principal investigator or the sponsor makes the subject unlikely to complete the study schedule of assessments.
(2) Any contraindication for MRI (including severe claustrophobia and any shrapnel or metal implants in the body that are not MRI compatible).
(3) Any contraindication for skeletal muscle needle biopsy (including current or recent use of anticoagulants or aspirin).
(4) Any ongoing medical problems in need of urgent medical care or hospitalization or scheduled procedures that will interfere with the schedule of assessments.
(5) Pregnancy.
(6) Any anticoagulants for at least one month and anti-platelet agents for at least 1 week before each biopsy are prohibited as they increase the risk of hematomas following skeletal muscle needle biopsy.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-04-2019
Enrollment:	6
Type:	Actual

Ethics review

Approved WMO Date:	29-01-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-02-2019
Application type:	Amendment
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	NL67007.091.18