A Phase 3 Global, Randomized, Double-Blind, Placebo-Controlled, 48-Week, ParallelGroup Study of the Efficacy and Safety of Losmapimod in Treating Patients with Facioscapulohumeral Muscular Dystrophy (REACH)

Published: 20-06-2022
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This study has been transitioned to CTIS with ID 2024-512737-33-00 check the CTIS register for the current data. Primary Objective:Part A:To evaluate the efficacy of losmapimod for the treatment of FSHD by demonstrating slowing of disease...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Musculoskeletal and connective tissue disorders congenital
Study type	Interventional

Summary

ID

NL-OMON53527

Source
ToetsingOnline

Brief title
1821-FSH-301

Condition

- Musculoskeletal and connective tissue disorders congenital

Synonym
muscular disease

Research involving

Human

Sponsors and support

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

Intervention

Keyword: congenital, Facioscapulohumeral Muscular Dystrophy, familial and genetic disorders, muscular disease

Outcome measures

Primary outcome

Primary Endpoints:

Deel A:

Change from baseline in average total RSA Q1--Q5 with 500 g wrist weight at

Week 48, where average is applied over both arms

Part B:

Safety and tolerability of long-term treatment with losmapimod, based on the

assessment of AEs, clinical laboratory tests, ECGs, vital signs, and physical

examinations.

Secondary outcome

Secondary Endpoints:

Part A:

1. PGIC at Week 48

2. Change from baseline compared to placebo in WB longitudinal composite MFI of

B muscles at Week 48

3. Relative change from baseline in average shoulder abductor strength by

hand-held quantitative dynamometry at Week 48

4. Change from baseline in Neuro-QoL UE at Week 48

5. Safety and tolerability, based on the assessment of adverse events, clinical

laboratory test, electrocardiograms (ECGs), and vital signs

Part B:

No secondary endpoints.

Study description

Background summary

Treatment of FSHD with losmapimod has demonstrated evidence of slowing of disease progression and/or improvement on clinical outcome assessments in people living with FSHD. Nonclinical studies have shown that losmapimod reduces the aberrant expression of double homeobox 4 (DUX4); the underlying cause of FSHD. Two Phase 2 clinical studies, a 48-week randomized controlled study (ReDUX4, FIS-002-2019) and a 52-week open-label study (OLS, FIS-001-2019) demonstrate evidence of benefit of treatment with losmapimod on structural and FSHD-relevant clinical endpoints that is recognized by patients, and a favorable safety and tolerability profile supporting continued development.

Study objective

This study has been transitioned to CTIS with ID 2024-512737-33-00 check the CTIS register for the current data.

Primary Objective:
Part A:
To evaluate the efficacy of losmapimod for the treatment of FSHD by demonstrating slowing of disease progression assessed by reachable workspace quantification of total relative surface area (RSA) Q1-Q5 with 500 g wrist weight averaged over both arms

Part B:
To assess the long-term safety and tolerability of losmapimod in patients with FSHD.

Secondary Objectives:
Part A:
1. To evaluate Patient Global Impression of Change (PGIC) relative to placebo
2. To evaluate efficacy of losmapimod to slow accumulation of fat in muscle by muscle fat infiltration (MFI) with whole body (WB) musculoskeletal (MSK) magnetic resonance imaging (MRI) relative to placebo
3. To evaluate relative change from baseline in shoulder strength by hand- held quantitative dynamometry relative to placebo.
4. To evaluate the change in Quality of Life in Neurological Disorders: Upper Extremities (Neuro-QoL UE) relative to placebo.
5. To assess safety and tolerability of losmapimod in patients with FSHD

Part B:
No Secondary objectives.

Study design

Part A of Study 1821-FSH-301 is a global, randomized, double-blind, placebo-controlled, parallel-group, multicenter study. Efficacy and safety of losmapimod will be evaluated in patients with FSHD over a 48-week treatment period. A total of approximately 230 patients with FSHD will be randomized 1:1 to receive losmapimod or placebo.

Upon completion of Part A, patients will have the option to rollover into Part B, the open-label extension. The long-term safety, tolerability, and efficacy of losmapimod will be evaluated in patients.

Intervention

For Part A: Losmapimod 15 mg will be administered orally twice daily with food. Placebo tablets will be identical in appearance to losmapimod tablets and will have the same excipients as the active tablets.

For Part B: Losmapimod 15 mg will be administered orally twice daily with food. There is no placebo.

Study burden and risks

Taking part in the study can have pros and cons.
The health of the subject may or may not improve in this study. But taking part will help the study doctors to get more insight into FSHD.

Taking part in the study can have these cons:
- The subject may experience side effects, adverse effects or discomforts from losmapimod or procedures.
- Taking part in the study will cost extra time.
- The subject have to comply with the study agreements.

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

Part A:
* Patients will have a diagnosis of FSHD1 or FSHD2 verified by genetic testing
* Patients will have a Clinical Severity Score of 2 to 4 (Ricci score; range 0 to 5) at screening. Patients who are wheelchair-dependent or dependent on walker or wheelchair for activities are not permitted to enroll in the study.

* Patients with screening total RSA (Q1-Q4) without weight in the dominant UE assessed by RWS >= 0.2 and <= 0.7.
* No contraindications to MRI.
* Patients (male and female) will be between the ages of 18 and 65 years at the time of consent, inclusive
* A female patient is eligible to participate if she is of non-child bearing potential, defined as pre-menopausal females with a documented hysterectomy, bilateral salpingectomy, or bilateral oophorectomy; if she is postmenopausal, defined as no menses for 12 months without an alternative medical cause; OR if of child-bearing potential, she is using a highly effective method for avoidance of pregnancy for the duration of dosing and until 90 days after the last dose of study drug.
* Male patients must agree to use one of the contraception methods listed in Section 5.5.1 of the protocol from the time of the first dose of study medication and until 90 days after the last dose of study drug.

Part B:
* Patient completed 48 weeks of treatment during Part A.
* Female patients of childbearing potential agree to continue using a highly effective method for avoidance of pregnancy for the duration of dosing and until 90 days after the last dose.
* Male patients must agree to use one of the contraception methods listed in Section 5.5.1 of the protocol from the time of the first dose of study medication and until 90 days after the last dose of study drug.

Exclusion criteria

Part A:
* Hx of any illness or any clinical condition that might confound the results of the study or pose an additional risk in administering study drug to the patient.
* Previously diagnosed cancer that has not been in complete remission for at least 5 years. Localized carcinomas of the skin and carcinoma in situ of the cervix that have been resected or ablated for cure are not exclusionary.
* For patients who are on drug(s) or supplements that may affect muscle function or that are included in the list of drugs presented in Appendix 3 of the Protocol: pt must be on a stable dose of that drug(s) or supplement for at least 3 months prior to the first dose of study drug and remain on that stable dose for the duration of the study. Changes to the dose or treatment discontinuation during the study can only be done for strict medical reasons by the treating physician with clear documentation and notification to the Sponsor.
* History of febrile illness within 5 days before the first study drug dose
* Known active opportunistic or life-threatening infections including HIV and hepatitis B or C
* Known active or inactive tuberculosis infection.

* Current acute liver disease or chronic liver disease as defined by any of the following: current ALT >=2 × upper limit of normal (ULN) or total bilirubin >1.5 × ULN (unless participant has Gilbert's syndrome characterized by the combination of total bilirubin < 3 × ULN, direct bilirubin within the normal range and normal ALT and AST, or the presence of mutations in the UDP glucuronosyltransferase 1 gene, indicative of Gilbert's syndrome); or Positive for hepatitis B or surface antigen; or Positive for hepatitis C antibody unless additional testing for hepatitis C viral RNA is negative, ALT is < 2 × ULN and total bilirubin is <= 1.5 × ULN, indicating inactive/resolved hepatitis C infection
* Known severe renal impairment (defined as a glomerular filtration rate of < 30 mL/min/1.73 m2).
* Standard 12-lead ECG demonstrating QTcF >450 msec for male patients and QTcF >470 msec for female patients at screening. If QTcF exceeds 450 msec for males or 470 msec for females, the ECG will be repeated 2 more times, and the average of the 3 QTcF values will be used to determine the patient's eligibility.
* History of cardiac dysrhythmias requiring anti-arrhythmia treatment(s); or history or evidence of abnormal ECGs
* Male patients with a female partner who is planning to become pregnant during the study or within 90 days after the last study drug dose
* Concomitant use of cytotoxic chemotherapy for cancer or known ongoing or anticipated use of chronic severe immunosuppressive agents.
* Positive pregnancy test or known to be pregnant or lactating or planning to become pregnant during study drug administration and until 90 days after last dose
* Any current mental condition (psychiatric disorder, senility or dementia)
* Patient has any condition possibly affecting drug absorption
* History of alcohol, analgesic/opioid, and/or illicit drug abuse, as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (American Psychiatric Association, 2013), in the last 6 months before screening or a positive test for drugs of abuse at screening. Use of CBD/THC is permitted
* Use of another IP within 30 days or 5 half-lives
* Current or anticipated participation in a natural hx study.
* Known hypersensitivity or intolerance to losmapimod or any of its excipients
* Previous participation in a Fulcrum-sponsored FSHD losmapimod study
* Abnormal laboratory results indicative of any significant medical disease

Part B:
* Any clinical condition that, in the opinion of the Investigator, might confound the results of the study or pose an additional risk in administering study drug to the patient.
* Male patients with a female partner who is planning to become pregnant during the study or within 90 days after the last study drug dose.
- Anticipated inability to comply with any study procedures, including participation in study visits.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-12-2022
Enrollment:	18
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Losmapimod
Generic name:	Losmapimod

Ethics review

Approved WMO Date:	20-06-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-08-2022
Application type:	First submission

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-09-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-09-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-10-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-02-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-05-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-08-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-02-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-04-2024
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
EU-CTR	CTIS2024-512737-33-00
EudraCT	EUCTR2022-000389-16-NL
ClinicalTrials.gov	NCT05397470
CCMO	NL81250.091.22