FSHD:

Clinical trials today

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CLINICAL TRIALS TODAY

What are clinical trials?

How to look for clinical trials to join

Ongoing Clinical trials

Future perspectives

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CLINICAL TRIALS 101

- A clinical trial is any research study that prospectively assigns **human participants** or groups of humans to one or more health-related **interventions** to evaluate the effects on **health outcomes** (World health organization definition)

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CLINICAL TRIALS 101

- Design (strategy)
  - Randomization
  - Blinding
- Inclusion/exclusion criteria
- Intervention
- Outcome measures

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How to look for clinical trials to join

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- ASK YOUR FOUNDATION!
- CLINICALTRIALS.GOV

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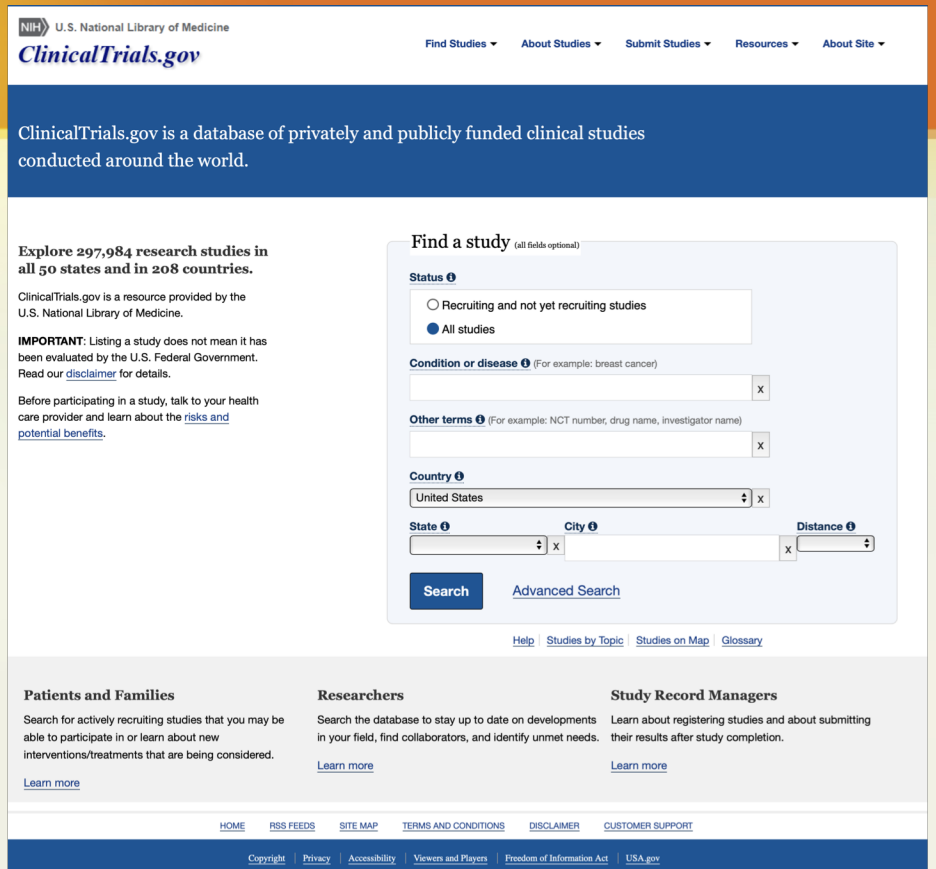

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Ongoing Clinical Trials for FSHD

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	☐	Recruiting	Study of Testosterone and rHGH in **FSHD**	• **Facioscapulohumeral Muscular Dystrophy**	• Drug: Testosterone Enanthate • Drug: Somatropin	• University of Rochester Rochester, New York, **United States**
2	☐	Recruiting	Magnetic Resonance Imaging and Spectroscopy Biomarkers for **Facioscapulohumeral Muscular Dystrophy**	• **Facioscapulohumeral Muscular Dystrophy**		• Doris Leung Baltimore, Maryland, **United States**
3	☐	Unknown †	Bone Health in **Facioscapulohumeral Muscular Dystrophy**	• **Facioscapulohumeral Muscular Dystrophy**		• Kennedy Krieger Institute, Johns Hopkins School of Medicine Baltimore, Maryland, **United States** • Concord Hospital Neurology Department, Hospital Road, Concord NSW 2139 Sydney, Australia
4	☐	Recruiting	Myotonic Dystrophy and **Facioscapulohumeral Muscular Dystrophy** Registry	• Myotonic Dystrophy • **Facioscapulohumeral Muscular Dystrophy** • Muscular Dystrophy • (and 6 more...)		• University of Rochester Medical Center, Department of Neurology Rochester, New York, **United States**
5	☐	Recruiting	Clinical Trial Readiness to Solve Barriers to Drug Development in **FSHD**	• **Facioscapulohumeral Muscular Dystrophy**	• Diagnostic Test: FSHD-specific functional rating scale • Device: Electrical Impedance Myography	• University of California Los Angeles Los Angeles, California, **United States** • University of Kansas Medical Center Kansas City, Kansas, **United States** • Kennedy Krieger Institute Baltimore, Maryland, **United States** • (and 5 more...)
6	☐	Active, not recruiting	Study of ACE-083 in Patients With **Facioscapulohumeral Muscular Dystrophy (FSHD)**	• **Facioscapulohumeral Muscular Dystrophy**	• Drug: ACE-083 • Drug: ACE-083 or placebo	• University of California Los Angeles Medical Center Los Angeles, California, **United States** • University of California Davis Medical Center Sacramento, California, **United States** • University of Colorado Aurora, Colorado, **United States** • (and 20 more...)

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ACE-083 in FSHD

Study Design Go to

Study Type :	Interventional (Clinical Trial)
Actual Enrollment :	55 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Primary Purpose:	Treatment
Official Title:	A Phase 2 Randomized, Double-Blind, Placebo-Controlled Study of ACE-083 in Patients With **Facioscapulohumeral Muscular Dystrophy**
Study Start Date :	November 2016
Estimated Primary Completion Date :	March 2020
Estimated Study Completion Date :	June 2020

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ACE-083 in FSHD

Ages Eligible for Study:	18 Years and older (Adult, Older Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Key Inclusion Criteria:

1. Age ≥ 18 years
2. Genetically-confirmed FSHD1 or FSHD2 (or a first-degree relative with genetically confirmed FSHD1 or FSHD2) and clinical findings meeting FSHD criteria
3. Part 1 TA cohorts:
    1. 6-minute walk distance (6MWD) ≥ 150 meters (without a brace)
    2. Mild to moderate weakness in left and/or right ankle dorsiflexion

    Part 1 BB cohorts:

    a. Mild to moderate weakness in left and/or right elbow flexion

    Part 2 TA cohorts:

    1. 6MWD ≥ 150 and ≤ 500 meters (without a brace)
    2. Mild to moderate weakness in left and right ankle dorsiflexion

    Part 2 BB cohorts:

    a. Mild to moderate weakness in left and/or right elbow flexion
4. Females of childbearing potential must have negative urine pregnancy test prior to enrollment and use highly effective birth control methods during study participation. Hormonal birth control use must be stable for at least 14 days prior to Day 1. Males must agree to use a condom during any sexual contact with females of childbearing potential while participating in the study even if he has undergone a successful vasectomy.

ACE-083 in FSHD

Key Exclusion Criteria:

1. Current/ active malignancy (e.g., remission less than 5 years duration), with the exception of fully excised or treated basal cell carcinoma, cervical carcinoma in-situ, or ≤ 2 squamous cell carcinomas of the skin
2. Symptomatic cardiopulmonary disease, significant functional impairment, or other co morbidities that in the opinion of the investigator would limit a patient's ability to complete strength and/or functional assessments on study
3. Renal impairment (serum creatinine ≥ 2 times the upper limit of normal [ULN])
4. Aspartate transaminase (AST) and/or alanine transaminase (ALT) ≥ 3 times ULN
5. Increased risk of bleeding (i.e., due to hemophilia, platelet disorders, or use of any anticoagulation/platelet modifying therapies up to 2 weeks prior to Study Day 1; low dose aspirin [≤ 100 mg daily] is permitted)
6. Major surgery within 4 weeks prior to Study Day 1
7. Chronic systemic corticosteroids (≥ 2 weeks) within 4 weeks before Study Day 1 and for duration of study; intra-articular/topical/inhaled therapeutic or physiologic doses of corticosteroids are permitted
8. Androgens or growth hormone within 6 months before Study Day 1 and for duration of study; topical physiologic androgen replacement is permitted
9. Any condition that would prevent MRI scanning or compromise the ability to obtain a clear and interpretable scan of the TA or BB muscles, as applicable (e.g., pacemaker, knee/hip replacement, or metallic implants)

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ACE-083 in FSHD

Experimental: ACE-083 (Part 2, DB-PC, IM tibialis anterior muscle) Double-Blind, Placebo-Controlled ACE-083 up to 250 mg IM (tibialis anterior muscle) or placebo, once every 3 weeks for up to 9 doses.	Drug: ACE-083 or placebo Recombinant fusion protein or normal saline.
Experimental: ACE-083 (Part 2, PL, IM tibialis anterior muscle) Open-Label ACE-083 up to 250 mg IM (tibialis anterior muscle) once every 3 weeks for up to 8 doses.	Drug: ACE-083 Recombinant fusion protein.
Experimental: ACE-083, (Part 2, DB-PC, IM biceps brachii muscle) Double-Blind, Placebo-Controlled ACE-083 up to 250 mg IM (biceps brachii muscle) or placebo, once every 3 weeks for up to 9 doses.	Drug: ACE-083 or placebo Recombinant fusion protein or normal saline.
Experimental: ACE-083 (Part 2, OP, biceps brachii muscle) Open-Label ACE-083 up to 250 mg IM (biceps brachii muscle), once every 3 weeks for up to 8 doses.	Drug: ACE-083 Recombinant fusion protein.

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ACE-083 in FSHD

Outcome Measures Go to

Primary Outcome Measures :

1. Safety and Tolerability (data collection on the incidence, nature and severity of adverse events). [Time Frame: From initiation of treatment (Study Day 1) to end-of-study visit (Study Day 141).]

   Adverse events will be recorded and coded in accordance with MedDRA v.20,0

Secondary Outcome Measures :

1. Estimation of systemic exposure to ACE-083 following local intramuscular administration. [Time Frame: From initiation of treatment (Study Day 1) to end-of-study visit (Study Day 141).]

   Bioanlaytical assay for the quantitative of ACE-083 in serum

2. Percent change from baseline in strength of injected muscle [Time Frame: From initiation of treatment (Study Day 1) to end of treatment visit.]

   Strength measurements by hand-held or fixed-system dynamometry (quantitative muscle testing).

3. Percent change from baseline in function of injected muscle [Time Frame: From initiation of treatment (Study Day 1) to end-of-study visit (Study Day 141).]

   Function assessed by a battery of motor function tests; 4-stair climb, 6-minute walk test, gait analysis and performance of the upper limb (PUL) test

4. Change from baseline in patient-reported outcome (PRO) measures [Time Frame: From initiation of treatment (Study Day 1) to end-of-study visit (Study Day 141).]

   PRO assessed by health-related quality of life and disease burden, as measured by the FSHD Health Index questionnaire (FSHD-HI).

Treatment strategies for FSHD

Table 1. FSHD therapeutic development

Therapeutic	Mechanism(s) of action	Tested in patients?	References
Anti-inflammatory	Immunosuppression Inhibit pathologic processes downstream of DUX4	Yes	(101,102)
Antioxidant	Prevent oxidative stress Inhibit pathologic processes downstream of DUX4	Yes	(103–106)
Antisense RNA	Enhance D4Z4 repression Inhibit DUX4 expression Inhibit pathologic processes downstream of DUX4	No	(19,39,76,77,94–96,107,108)
BET bromodomain inhibitor	Enhance D4Z4 repression Inhibit DUX4 expression	No	(97)
Beta-2 adrenergic agonist	Increase muscle strength/mass Enhance D4Z4 repression Inhibit DUX4 expression	Yes	(97,109–111)
Calcium channel blocker	Restore calcium dysregulation Inhibit pathologic processes downstream of DUX4	Yes	(112,113)
Exercise	Increase muscle strength/mass	Yes	(114–116)
GSK3β inhibitor	Enhance D4Z4 repression Inhibit DUX4 expression	No	(40)
Myostatin inhibitor	Increase muscle strength/mass	Yes	(117,118)
Steroid	Increase muscle strength/mass	Yes	(119)
Tissue transplantation	Enhance muscle regeneration Block DUX4 spreading	Yes	(120,121)
Tyrosine kinase inhibitor	Enhance muscle regeneration Inhibit pathologic processes downstream of DUX4	No	(98)
Unknown	Enhance D4Z4 repression Inhibit DUX4 expression Block DUX4 activity Block DUX4 spreading Inhibit pathologic processes downstream of DUX4	No	(77,99)

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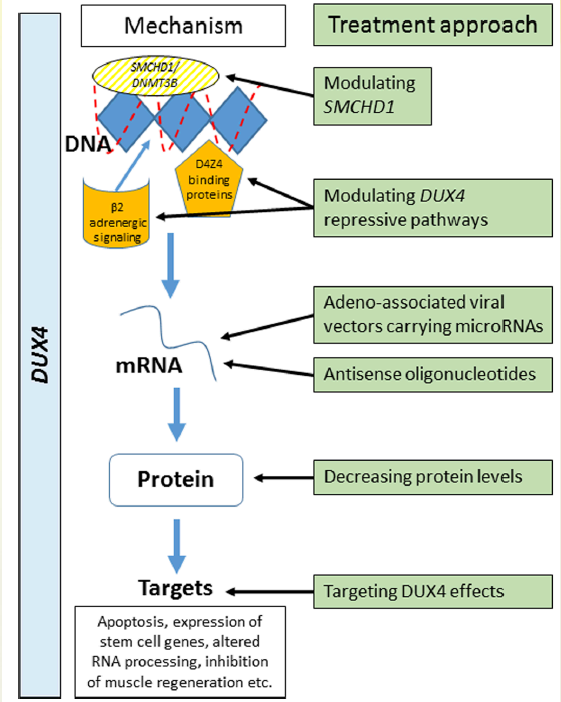
Treatment strategies



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QUESTIONS?

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