Outcome measures in Duchenne Muscular Dystrophy: A natural history study

Hub Summary

With so many new therapies emerging for DMD, it is important we understand the natural history of the disease. This natural history study will assess the natural history of DMD sing a selection of assessment tools. The aim is to obtain natural history data to capture disease progression linking the ambulant and non-ambulant phases of DMD. This study will also provide an insight into the relationship between different assessment tools which are used in the clinic.

Study Number: NCT02780492

Description by University College, London

This study will offer a comprehensive natural history of DMD including novel outcome measures, allowing the capture of disease progression and exploration of the relationship between different assessment tools.

Novel emerging therapies for Duchenne Muscular Dystrophy (DMD) require a deeper understanding of DMD natural history. This study aim to assess the natural history of DMD through a composite assessment tool capable of capturing disease progression linking ambulant and non-ambulant phases of the disease.

With a recruitment target of 80 DMD patients across 5 centres (London, Newcastle, Paris, Leiden, Nijmegen), subjects are assessed 6 monthly according to a shared protocol. Assessments include 6-minute walk distance (6MWD), North Star Ambulatory Assessment (NSAA), Performance of Upper Limb (PUL) and MyoSet (myogrip, myopinch and moviplate). Both ambulant and non-ambulant subjects undergo upper limb evaluation and respiratory function test including forced vital capacity (FVC), maximum inspiratory and expiratory pressures (MIP/MEP). A subgroup of patients performs annual whole body DEXA scan. An imaging sub-study will aim to characterize muscle (upper/lower limb) and brain MRI.

The investigators will analyze the longitudinal data for the different assessment tools and explore correlations among them.

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Primary Outcome Measures

- Disease progression [Time Frame: up to 4 years]

Evaluate disease progression from ambulant to non-ambulant patients through a composite assessment tool

Can I take part?

Inclusion Criteria

For non-ambulant patients:

- Children and teenagers aged between 5 and 18 years with DMD, who have lost the ability to walk 10 meters with no support
- The diagnosis of DMD must be documented by genetic testing. If a muscle biopsy is available, it should contain less than 10% of revertant fibres
- Patients should have deletions amenable of skipping of exons 51 or 53 or 45 or 44 or 46 or 50 or 52
- Patients should be capable of sitting upright in a wheelchair for at least an hour
- Patients should be stable from a respiratory point of view. Artificial ventilation with either Bipap or tracheostomy is not a contraindication to the study.
- Informed consent signed by a parent/legal guardian (or by the patient if 16 years of age).
- In France, a subject will be eligible for inclusion in this study only if either affiliated

Trial Status
Trial complete

UK Locations
London - GOSH, Trial complete/terminated, Newcastle, Trial complete/terminated

Trial Sponsor
University College, London

Age
5-18

Mutation Specific
Non-mutation specific therapies

Muscle Biopsy
No Muscle Biopsy Required

MRI
Yes

Phase
n/a

Length Of Participation
TBC (Up to 4 years)

Recruitment Target
80

Ambulatory
Ambulant and non-ambulant, Both ambulant and non-ambulant subjects required.

Therapeutic Category
Natural history study

to, or a beneficiary of, a social security category.

For ambulant patients:

- Ambulant children from 5 years old and teenagers with DMD, and potential candidates for future genetic therapies with antisense oligomer (AO) exon skipping
- The diagnosis of DMD must be documented by MLPA or a standard genetic test for the disorder, genotypically confirmed to have an out-of-frame deletion(s) that could be corrected by skipping exon 51 or 53 or 45 or 44 or 46 or 50 or 52
- If a muscle biopsy is available less than 10% revertant fibres
- Ability to walk independently for at least 75 meters in 6 minutes at recruitment.
- Patients should receive the standard of care for DMD as recommended by the NorthStar UK and TREAT-NMD (i.e.: on glucocorticoids treatment)
- Sufficiently preserved pulmonary function (FVC >30%) and absence of symptoms of cardiac failure
- Informed consent signed by a parent/legal guardian (or by the patient if 16 years of age)
- In France, a subject will be eligible for inclusion in this study only if either affiliated to, or a beneficiary of, a social security category.

For healthy volunteers and disease controls:

- Participant are able to provide informed consent/assent for taking blood samples and/or performing limb MRI and/or physiotherapy assessment of the upper limb function
- Participants have a neuromuscular disease that is not Duchenne Muscular Dystrophy or are a healthy volunteer with no neuromuscular disease
- Able to have a blood sample taken

Exclusion Criteria

For non-ambulant patients:

- Patients who are currently involved in interventional clinical trials aimed at restoring dystrophin will be excluded, as their data could not be used to establish natural history of the disease (participation in a previous interventional clinical trial prior to 6 months from being recruited in the study is not an exclusion criterion)
- Patients with severe intellectual impairment, who would be unable to cooperate with examination
- Patients/families the investigators anticipate may have emotional/ psychological problems if recruited into a natural history study
- Symptomatic cardiac failure
- Recent (< 6 months) upper limb surgery or trauma
- Anticipated surgery for anytime during the duration of the study
- None of the current treatments for DMD are exclusion criteria
- For the MRI sub-study, patients with metal/metallic surgically inserted equipment incompatible with MRI scan will be excluded as well as patients suffering from claustrophobia.

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For contact details and to find out more, please refer to dmdhub.org.

Duchenne UK

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