Tamoxifen (TAMDMD)

Tamoxifen in Duchenne Muscular Dystrophy

Hub Summary

PLEASE NOTE: Recruitment for Group A (ambulant DMD patients) has been completed but recruitment for Group B (non-ambulant, steroid-naive DMD patients) is still open. Please contact the sites if you would like to take part.

This placebo control, 48-week clinical trial will look at the treatment with Tamoxifen for both ambulant and non-ambulant patients with DMD. Tamoxifen has been used to treat breast cancer since the 1980s and is also used for hormonal disorders in pre-pubescent boys. Preliminary data in the DMD mouse model demonstrated that Tamoxifen reduced fibrosis, increased the thickness of muscle fibres, and resulted in a delay in disease progression.

Study Number: NCT03354039

Description by University Children's Hospital Basel

A randomised, double blind, placebo controlled, 48-week clinical trial with a core population (group A) of 79 ambulant 6.5 to 12 years old Duchenne's muscular dystrophy (DMD) patients that are under stable standard treatment of care with glucocorticoids. Furthermore, the investigators plan to include 16-20 non-ambulant patients who do not receive glucocorticoids (as parallel group B), 10 to 16 years old, to obtain efficacy and safety data in a broader DMD population. All patients will receive 20 mg of tamoxifen (TAM) or placebo once daily during 48 weeks.

This is a 48-week multicentre, parallel, randomised, double-blind, placebo controlled phase 3 safety and efficacy trial. There are two treatment arms: Tamoxifen (verum) and placebo (control), with treatment allocation of 1:1.

The investigators plan to screen at least 79 and to enroll at least 71 ambulant DMD patients aged between 6.5 and 12 years (group A) and 16 - 20 non-ambulant DMD patients aged between 10 and 16 years (group B). In order to reach statistical power, 60 ambulant patients (group A) need to complete the trial. Treatment with 20 mg Tamoxifen once daily will be given for the total trial duration of 48 weeks.

Only patients with glucocorticoids (standard treatment of care) will be included in group A (ambulant patients) and only non-glucocorticoid users in group B. At baseline, 24 weeks and at the end of the study clinical, laboratory, and MRI measurements will be performed. These include the Motor Function Measure (MFM) scale, timed function tests, the 6 minute walking distance, quantitative muscle testing (QMT) and quantitative thigh muscle MRI, questionnaires. Physiotherapeutical assessments will be performed at every visit. A physical examination, an ECG, vital signs as well as safety laboratory blood analyses will also be performed at every visit. Furthermore, an x-ray of the hand and a dual energy x-ray absorptiometry (DEXA)-scan will be performed at baseline and at the end of the study.

Primary Outcome Measures

- Reduction of disease progression [Time Frame: Baseline to week 48]

To test if tamoxifen treatment, compared to placebo, reduces the progression of the disease in 6.5-12 years old ambulant DMD patients (Group A) by at least 50% (using the MFM D1 subscore as primary clinical endpoint).

Secondary Outcome Measures

- Muscle function measured by D2 MFM subscore
- Muscle function measured by D3 MFM subscore
- Muscle function measured by North Star Ambulatory Assessment
- Muscle function measured by proximal upper limb function
- Muscle function measured by 6-minute walking distance in meter
- Muscle function measured by 10-meter walking time in seconds
- Muscle function measured by time to rise from lying on the floor / supine up in seconds
- Muscle force measured by quantitative muscle testing (using Myogrip)

Trial Status
Recruiting

UK Locations
Alder Hey, Recruiting,
Glasgow, Recruiting,
Leeds, Recruiting

Trial Sponsor
University Children's Hospital Basel

Age
78 months to 16 years

Mutation Specific
Non-mutation specific therapies

Muscle Biopsy
No Muscle Biopsy Required

MRI
Yes

Phase
3

Length Of Participation
48 weeks

Recruitment Target
99

Ambulatory
Ambulant and non-ambulant

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- Muscle Degeneration measured by MRI

Other Outcome Measures

- Patient reported outcome measured by Personal Adjustment and Role Skills Scale (PARS III) questionnaire

Can I take part?

Inclusion Criteria

Group A (ambulant patients)

- Documented diagnosis of DMD by mutation analysis in the dystrophin gene or by substantially reduced levels of dystrophin protein (i.e. absent or <5% of normal) on Western blot or immunostaining
- Stable treatment with glucocorticoids >6 months (no significant change in dosage (>0.2mg/kg)) at screening; dosing adaptations according to weight change are allowed
- Male gender
- 6.5 to 12 years of age at time of screening
- weight >15kg
- ambulant patients
- able to walk at least 350 meters in 6-minute walking distance test without assistance
- MFM D1 subdomain of the MFM scale >40% at screening
- Ability to provide informed consent and to comply with study requirements

Group B (non-ambulant patients)

- Documented diagnosis of DMD by mutation analysis in the dystrophin gene or by substantially reduced levels of dystrophin protein (i.e. absent or <5% of normal) on Western blot or immunostaining
- Not using glucocorticoids for >6 months
- Male gender
- Non-ambulant patients (walking distance less than 10 meters)
- 10 to 16 years of age at time of screening
- Ability to provide informed consent and to comply with study requirements

Exclusion Criteria

- Known individual hypersensitivity or allergy to tamoxifen
- Female gender
- Use of tamoxifen or testosterone within the last 3 months
- Known or suspected malignancy
- Other chronic disease or clinically relevant limitation of renal, liver or heart function
- Known or suspected non-compliance
- Any injury which may impact functional testing, e.g. upper or lower limb fracture
- Planned or expected spinal fusion surgery during the study period (as judged by the Investigator; i.e. due to rapid progressing scoliosis), previous spinal fusion surgery is allowed if it took place more than 6 months prior to screening.
- Inability to follow the procedures of the study, e.g. due to language problems, psychological disorders of the participant/parents (as judged by the investigator)
- Concomitant participation in any other interventional trial (and up to 3 months prior to screening)

Group A:

- Glucocorticoid naïve patients
- Start of glucocorticoid treatment or change in dosage <6 month prior to screening (dosing adaptations according to weight change are allowed)

Group B:

- Glucocorticoid treated patients or patients that stopped glucocorticoid treatment <6 month prior to screening
- Assisted ventilation of any kind necessary

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

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