Italfarmaco- Givinostat (EPIDYS)

Clinical Study to Evaluate the Efficacy and Safety of Givinostat in Ambulant Patients with Duchenne Muscular Dystrophy (EPIDYS)

Hub Summary

This study will compare the change in stair climb test and other functional tests in patients taking givinostat and patients taking a placebo. Givinostat has potential anti-inflammatory, antifibrotic and proregenerative effects.

Please note this protocol was amended early 2019.

Study Number: NCT02851797

Description by Italfarmaco

Randomised, double blind, parallel group and placebo controlled study. A total of 242 male ambulant subjects will be randomised 2:1 (givinostat:placebo).

Subjects will be stratified for their concomitant use of steroids in 4 strata:

- Deflazacort daily regimen
- Deflazacort intermittent regimen
- Other steroids daily regimen
- Other steroids intermittent regimen.

The study duration is planned for 19 months. Patients who will complete 18 months of treatment will be asked to continue givinostat treatment in a open-label long term study, regardless their ambulatory ability (NCT03373968).

Givinostat or placebo oral suspension (10 mg/mL) will be administered orally as 2 oral doses daily while the subject is in fed state, according to the child's weight.

Study drug should be permanently stopped if any of the following occur:

- severe drug-related diarrhoea;
- any drug-related Serious Adverse Event;
- QTcF >500 msec;
- platelets count <50 x 109/L.

Study drug should be temporarily stopped if any of the following occur:

- platelets count <75 x 109/L but >50 x 109/L (the treatment should be temporarily stopped and a platelets count has to be performed and re-tested until platelets will be normalized);
- moderate or severe diarrhoea.
- Triglycerides >300 mg/dL (3.42 mmol/L) in fasting conditions (the treatment should be temporarily stopped and triglycerides has to performed and re-tested bi-weekly until triglycerides will return below 300 mg/dL)

In case the study drug was temporarily stopped, the study drug can be resumed at level 1/3 or 20% smaller than the one at which the Adverse Event leading to temporary stop occurred, based on protocol indication.

Two interim analyses are planned and will be conducted by the IDMC in order to ensure study integrity.

Primary Outcome Measures

- Mean change in 4 standard stairs climb over 18 months.

Trial Status
Trial complete

UK Locations
London - GOSH, Trial complete/terminated, Alder Hey, Trial complete/terminated, Newcastle, Trial complete/terminated, Oswestry, Trial complete/terminated

Trial Sponsor
Italfarmaco

Age
6-17

Mutation Specific
Non-mutation specific therapies

Muscle Biopsy
No Muscle Biopsy Required

MRI
Yes

Phase
3

Length Of Participation
19 Months

Recruitment Target
242

Ambulatory
Ambulant

Therapeutic Category
Inflammation and fibrosis

The primary endpoint is the mean change in the 4 standard stairs climb test results before and after 18 months of treatments of givinostat versus placebo.

Secondary Outcome Measures

- Other functional test as 6MWT (mean change)
- Time to rise from floor (mean change)
- Magnetic Resonance Spectroscopy (mean change in fat friction of vastus lateralis muscles at MRS).
- NSAA total score (mean change)
- Triglycerides >300 mg/dL (3.42 mmol/L) in fasting conditions (the treatment should be temporarily stopped and triglycerides has to performed and re-tested bi-weekly until triglycerides will return below 300 mg/dL)

Can I take part?

Inclusion Criteria

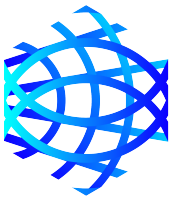
- Are an ambulant male aged 6 years or over at randomisation with DMD characteristic clinical symptoms or signs (e.g., proximal muscle weakness, Gowers' maneuver, elevated serum creatinine kinase level) already present at screening.
- Have DMD diagnosis confirmed by genetic testing.
- Are able to give informed assent and/or consent in writing signed by the subject and/or parent/legal guardian (according to local regulations).
- Are able to complete 2 Four Stairs Climb test (4SC) screening assessments; the results of these tests must be within ±1 second of each other.
- Have the mean of 2 screening 4SC assessments < or = to 8 seconds.
- Have time to rise from floor of > or =3 or <10 seconds at screening.
- Have manual muscle testing (MMT) of quadriceps at screening > or = Grade -3.
- Have used systemic corticosteroids for a minimum of 6 months immediately prior to the start of study treatment, with no significant change in corticosteroids type or dosage or dosing regimen (excluding changes related to body weight change) for a minimum of 6 months immediately prior to start of study treatment and a reasonable expectation that dosage and dosing regimen will not change significantly for the duration of the study

Exclusion Criteria

- Have exposure to another investigational drug within 3 months prior to the start of study treatment;
- Have exposure to idebenone within 3 months prior to the start of study treatment;
- Have exposure to any dystrophin restoration product (e.g., Ataluren, Exon skipping) within 6 months prior to the start of study treatment;
- Use of any pharmacologic treatment, other than corticosteroids, that might have had an effect on muscle strength or function within 3 months prior to the start of study treatment (e.g., growth hormone); Vitamin D, calcium, and any other supplements will be allowed as long as their intake has been stable for 3 months prior to the start of study treatment; Testosterone will also be allowed if it is used as a replacement therapy for the treatment of delayed puberty, and testosterone dose and regimen have been stable for at least 6 months and circulating testosterone levels are within the normal ranges for the subject’s age.
- Have surgery that might have an effect on muscle strength or function within 3 months before study entry or planned surgery at any time during the study;
- A loss of >30 degrees of plantar flexion from the normal range of movement at the ankle joint due to contracture.
- Change in contracture treatment such as serial casting, contracture control devices, night splints, stretching exercises (passive, active, self) within 3 months prior to enrolment, or expected need for such intervention during the study;
- Have presence of other clinically significant disease, which, in the Investigator's opinion, could adversely affect the safety of the subject, making it unlikely that the course of treatment or follow-up would be completed, or could impair the assessment of study results;
- Have a diagnosis of other uncontrolled neurological diseases or presence of relevant uncontrolled somatic disorders that are not related to DMD

- Have platelets count, White Blood Cell and Haemoglobin at screening <Lower Limit of Normal (LLN)
- Have symptomatic cardiomyopathy or heart failure (New York Heart Association Class III or IV) or left ventricular ejection fraction <50% at screening;
- Have a current or history of liver disease or impairment;
- Have inadequate renal function, as defined by serum Cystatin C >2 x the upper limit of normal (ULN);
- Have a positive test for hepatitis B surface antigen, hepatitis C antibody, or human immunodeficiency virus at screening;
- Have a baseline QTcF >450 msec, or history of additional risk factors for torsades de pointes (e.g., heart failure, hypokalemia, or family history of long QT syndrome);
- Have a psychiatric illness/social situations rendering the potential subject unable to understand and comply with the muscle function tests and/or with the study protocol procedures;
- Have any known allergic reaction to givinostat or any of its excipients.
- For the subgroup of subjects who will undergo MRI and MRS (i.e., MR Cohort):
- Have contraindications to MRI or MRS (e.g., claustrophobia, metal implants, or seizure disorder).
- Have Triglycerides > 300mg/dL (3.42 mmol/L) in fasting conditions at screening visit

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



Duchenne UK

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