Italfarmaco - ULYSSES

Randomised, Double-blind, Placebo-controlled, Multicentre Study to Evaluate the Efficacy, Safety and Tolerability of Givinostat in Non-ambulant Patients With Duchenne Muscular Dystrophy (ULYSSES)

Hub Summary

The main objective of this study is to demonstrate the efficacy of givinostat in reducing muscle decline in non-ambulant patients aged 9-17 with Duchenne Muscular Dystrophy. Additional objectives are the evaluation of safety, tolerability of the drug and further exploration of efficacy of givinostat in non-ambulant DMD population.

Study Number: NCT05933057

Description by Italfarmaco

This is a randomised, double-blind, placebo-controlled, multicentre study to evaluate the efficacy, safety, and tolerability of givinostat in non-ambulant male paediatric (aged 9 to <18 years) patients with DMD. It is anticipated that 138 patients will be randomised 2:1 to givinostat or placebo and will be treated for 18 months with an oral suspension of study drug twice daily (bid) in a fed state.

Primary Objective of the study is to demonstrate the efficacy of givinostat in reducing muscle decline in non-ambulant DMD patients, as measured by Performance of the Upper Limb (PUL) 2.0.

Secondary Objectives of the study are to evaluate the safety and tolerability of givinostat in non-ambulant DMD patients, and to further explore the efficacy of givinostat in non-ambulant DMD patients.

Primary Outcome Measures

Change of Performance of Upper Limb 2.0 (PUL) total score after 18 months of treatment of givinostat compared to placebo group. [Time Frame: Baseline and 18 months]

The PUL examines 3 major "dimensions" of upper extremity function: shoulder, middle, and distal functions. It includes 21 scored items; a score of 42 (12 for shoulder; 17 for mid-level, and 13 for distal) indicates the highest level of independent function and 0 the lowest.

Other Outcome Measures

Can I take part?

Inclusion Criteria

1. Children and adolescent males aged 9 to <18 years at screening
2. Are able to give informed assent (ie, parent /legal guardian) and/or consent, according to local regulations
3. A genetic diagnosis of DMD
4. Non-ambulant defined as being wheelchair bound and:
    1. Unable to perform the 10-meter walk/run test (10MWT), or
    2. Unable to complete the 10MWT in 30 seconds or less, without any support or devices
5. Performance of the Upper Limb test (PUL version 2.0) entry item scores 3 to 6
6. If on medication for DMD-associated cardiomyopathy (eg, ACE inhibitor, -blocker,

Trial Status
Fully recruited

UK Locations
Glasgow, Fully recruited,
Newcastle, Fully recruited,
Oxford, Fully recruited

Trial Sponsor
Italfarmaco

Phase
3

Length Of Participation
18 months

Recruitment Target
138

Ambulatory
Non-ambulant

Therapeutic Category
Interventional

Age
9-17

Mutation Specific
All treatment types

diuretics), stable for 1 month immediately prior to start of study treatment, if any

7. Stable corticosteroids, defined as:
    1. Receiving systemic corticosteroids for a minimum of 6 months immediately prior to start of study treatment
    2. No significant change in dose or dosing regimen (except for adjustments due to body weight change) for a minimum of 6 months immediately prior to start of study treatment
8. Willing to use adequate contraception. Effective contraceptive methods must be used from randomisation visit through 3 months after the last dose of study drug.

Exclusion Criteria

1. Exposure to another investigational drug within 3 months prior to start of study treatment
2. Have exposure to any dystrophin restoration product (eg, Ataluren, Exon skipping) within 6 months prior to the start of study treatment
3. Having received any gene therapy (eg, Adeno-associated viruses Micro-dystrophin delivery) prior to start of study treatment
4. Use of any pharmacologic treatment or supplement, other than corticosteroids, that might have had an effect on muscle strength or function within 3 months prior to the start of study treatment (eg, growth hormone)
5. Use of testosterone, unless used as a replacement therapy for the treatment of delayed puberty. The testosterone dose and regimen should be stable within 6 months prior to the start of study treatment, and circulating testosterone levels should be within the normal ranges for the patient's age
6. Elbow-flexion contractures >30° in the dominant arm

7. Inability to perform consistent PUL 2.0 measurement within ±2 points without shoulder domain or within ±3 points with shoulder domain during paired testing at screening
8. Forced Vital Capacity (FVC) % of predicted <40%
9. Requirement for daytime ventilator assistance. Note: Night ventilator assistance and use of bi-level positive airway pressure therapy is allowed
10. Episode of respiratory failure within the 8 weeks prior to screening
11. Symptomatic cardiomyopathy or heart failure and/or left ventricular ejection fraction <45%
12. Baseline corrected QT interval using Fredericia's formula (QTcF) >450 msec (as the mean of 3 consecutive readings 5 minutes apart) or history of additional risk factors for torsades de pointes (eg, heart failure, hypokalaemia, or family history of long QT syndrome)
13. Major surgical procedure (including scoliosis surgery) planned within 1 year of the start of study treatment
14. Poorly controlled asthma or underlying lung disease such as bronchitis, bronchiectasis, emphysema, recurrent pneumonia that in the opinion of the Investigator might impact respiratory function
15. Platelets, white blood cells and/or haemoglobin < lower limit of normal (LLN) at screening (Note: for abnormal screening laboratory test results <LLN, the platelets count, white blood cell, and haemoglobin will be repeated once; if the repeat test result is still <LLN, the patient should be excluded)
16. Fasting triglycerides >300 mg/dL (3.42 mmol /L) at screening (Note: if the value is >300 mg /dL, the triglycerides will be repeated once; if the repeated test result is still >300 mg/dL, the patient should be excluded)
17. Current or history of liver disease or impairment, including but not limited to a baseline elevated total bilirubin (ie, >1.5 × upper limit of normal [ULN]), unless secondary

to Gilbert disease or pattern consistent with Gilbert disease

18. Inadequate renal function, as defined by serum Cystatin C result >2 × ULN (Note: if the value is >2 × ULN, the serum Cystatin C will be repeated once; if the repeated test result is still >2 × ULN, the patient should be excluded)
19. Positive test for hepatitis B surface antigen, hepatitis C antibody, or human immunodeficiency virus at screening
20. Hypersensitivity to any component of study medication
21. Sorbitol intolerance or malabsorption, or the hereditary form of fructose intolerance
22. Diagnosis of other uncontrolled neurological diseases or presence of relevant uncontrolled somatic disorders that are not related to DMD, based on Investigator judgement
23. Psychiatric illness or social situations rendering the potential patient unable to understand and comply with the muscle function tests and/or with the study protocol procedures, based on Investigator judgement
24. Have contraindications to Magnetic Resonance Imaging (MRI) scan (eg, claustrophobia, metal implants, or uncontrolled seizure disorder), based on Investigator's judgement.