Antisense - ATL1102

A Multicentre, Randomised, Double-blind, Placebo-controlled and Open Label Extension Study to Assess the Efficacy, Safety, and Pharmacokinetic Profile of ATL1102 in Non-ambulatory Participants With Duchenne Muscular Dystrophy

Hub Summary

This Phase IIb study is a two part, multicenter study to evaluate the efficacy, safety, pharmacokinetics and pharmacodynamics of ATL1102 in non-ambulant boys with Duchenne Muscular Dystrophy aged 10 to 17 years old. The study includes a randomised, double-blind, placebo-controlled treatment period (Part A), followed by an open labelled treatment period (Part B).

Study Number: NCT05938023

Description by Antisense Therapeutics Limited

This Phase IIb study is a two part, multicenter study to evaluate the efficacy, safety, pharmacokinetics and pharmacodynamics of ATL1102 and will enroll 45 non-ambulant boys with Duchenne Muscular Dystrophy (DMD) aged 10 to <18 years old.

During the 24 week randomised, double-blind, placebo-controlled treatment period (Part A) participants will be enrolled and randomised to receive either ATL1102 25mg, ATL1102 50mg or matched placebo in a 1:1:1 ratio given as a weekly subcutaneous injection.

Participants will then continue to the 24 week Open Labelled Treatment Period (Part B) and continue to receive ATL1102 25mg or ATL1102 50mg for a further 24 weeks. Participants on placebo in Part A will transition to ATL1102.

The study will consist of a 4 week screening period, 24 week randomised, double-blind, placebo-controlled treatment period (Part A), 24 week open label treatment period (Part B) and 16 week follow up period.

Primary Outcome Measures

1. Change in the Performance of Upper Limb (PUL) 2.0 score from baseline to Week 25 (blinded treatment period). [Time Frame: 25 weeks]

   The PUL is an assessment used to evaluate the upper limb strength for individuals with DMD where a higher score indicates a better outcome with a minimum of 0 and a maximum score of 42

2. Change in the Performance of Upper Limb (PUL) 2.0 score from Week 25 to Week 49 (open label treatment period). [Time Frame: 49 weeks]

   The PUL is an assessment used to evaluate the upper limb strength for individuals with DMD where a higher score indicates a better outcome with a minimum of 0 and a maximum score of 42

3. Change in the Performance of Upper Limb (PUL) 2.0 score from baseline to Week 49 (combined treatment period). [Time Frame: 49 weeks]

   The PUL is an assessment used to evaluate the upper limb strength for individuals with DMD where a higher score indicates a better outcome with a minimum of 0 and a maximum score of 42

4. Safety measured by the incidence and frequency of adverse events, serious adverse events and suspected unexpected adverse events from baseline to

Trial Status
Recruiting

UK Locations
London - GOSH, Recruiting, Alder Hey, Recruiting, Birmingham, Recruiting, Glasgow, Recruiting, Leeds, Recruiting, Manchester, Recruiting, Oswestry, Recruiting

Trial Sponsor
Antisense Therapeutics Limited

Age
10 - 17

Mutation Specific
Non-mutation specific therapies

Muscle Biopsy
No Muscle Biopsy Required

MRI
No

Phase
Phase 2

Length Of Participation
69 weeks

Recruitment Target
45

Ambulatory
Non-ambulant

dmdhub.org

Week 65 [Time Frame: 65 weeks]

An Adverse Event is any untoward medical occurrence in a participant and does not necessarily have to have a causal relationship with the intervention.

Secondary Outcome Measures

1. Change in the grip strength of the hand from baseline to Week 25 using a handheld dynamometer tool (MyoGrip) (blinded treatment period). [Time Frame: 25 weeks]

   The handheld dynamometer tool (MyoGrip) use strain gauge technology to measure the hand strength in Kilograms exerted by the participants with higher recordings indicating greater hand strength.

2. Change in the pinch strength of the fingers from baseline to Week 25 using handheld dynamometer tool (MyoPinch) (blinded treatment period). [Time Frame: 25 weeks]

   The handheld dynamometer tool (MyoPinch) use strain gauge technology to measure the pinch strength of the fingers in Kilograms exerted by the participants with higher recordings indicating greater hand strength.

3. Change in the respiratory function assessed by Forced Vital Capacity (FVC) from baseline to Week 25 (blinded treatment period). [Time Frame: 25 weeks]

   The percent predicted for Forced Vital Capacity (FVC%p) will be calculated at multiple timepoints after respiratory function is assessed using spirometry tests

4. Change in the respiratory function assessed by peak expiratory flow (PEF) from baseline to Week 25 (blinded treatment period). [Time Frame: 25 weeks]

   The percent predicted for peak expiratory flow (PEF%p) will be calculated at multiple timepoints after respiratory function is assessed using spirometry tests

5. Change in the Paediatric Quality of Life (PedsQL™) questionnaire Duchenne Muscular Dystrophy (DMD) Module from baseline to Week 25 (blinded treatment period). [Time Frame: 25 weeks]

   Health related quality of life is assessed by percentage of change in the score collected in the Paediatric Quality of Life (PedsQL™) Duchenne Muscular Dystrophy (DMD) Module for participants and parents at multiple timepoints. A higher score indicates a better health related quality of life with a minimum of 0 and a maximum score of 100.

6. Other Secondary Outcome Measures can be found on Clinicaltrial.gov

Other Outcome Measures

Changes in lymphocyte populations to assess pharmacodynamic effects of ATL1102 from baseline to Week 57 [Time Frame: 57 weeks]

Lymphocyte population (cells/L) including cells expressing CD49d will be evaluated at multiple timepoints during the study utilizing chip cytometry.

Can I take part?

Inclusion Criteria

- Has a clinical diagnosis of DMD confirmed by validated genetic testing
- Is considered to be non-ambulatory, defined as unable to walk 10 meters without assistance or help at Screening.
- Male aged 10 to less than 18 years, at the time of Screening.
- Body weight of at least 25 kg at Screening.
- If receiving corticosteroid therapy, therapy was initiated at least six months prior to the baseline visit and a stable daily dose for at least 3 months prior to baseline
- Participant has a Performance of Upper Limb Module for DMD 2.0 (PUL 2.0) Entry Item A score ≥2.
- Able to perform spirometry and has sufficient Respiratory function defined as

reproducible percent predicted FVC ≥50%.

- Has adequate cardiac function defined as left ventricular ejection fraction (LVEF) ≥45% by echocardiogram and if receiving cardiac medication, must be currently on a stable regimen and doses of cardiac therapy (at least 3 months prior to baseline Day 1)
- Participant and their parent/guardian/carer are willing and able to comply with scheduled visits, study medication administration and study procedures.

Exclusion Criteria

- Participation in another clinical trial (non-interventional) or administration of any investigational product or experimental product within 12 weeks or 5 half-lives (whichever is longer) preceding Day 1.
- Exposure to more than 3 investigational products within the 12 months prior to Day 1.
- History of clinically significant bleeding or coagulation abnormalities or clinically significant abnormal coagulation parameters.
- Currently receiving antiplatelet or anticoagulant therapy or has taken medication with an antiplatelet or anticoagulant effect within 4 weeks prior Day 1
- Any evidence of clinically significant structural or functional heart abnormality (cardiomyopathy that is managed by ACEi or beta blockers is acceptable provided the LVEF inclusion criterion is met).
- Known history of or a positive test for hepatitis B surface antigen (HBsAg), hepatitis C (HCV) antibodies, human immunodeficiency virus (HIV) antibodies at Screening.
- Evidence of renal impairment and/or cystatin C >1.4 mg/L.
- Received a live vaccine (including intranasal influenza vaccine) within 4 weeks prior to Day 1 or planned live vaccination during the study period.
- Asthma (if requiring regular medication), bronchitis/chronic obstructive pulmonary disease (COPD), bronchiectasis, emphysema, pneumonia or the presence of any non-DMD respiratory illness that affects PEF and FVC or other respiratory measures.
- Requires day-time assisted mechanical or non-invasive ventilation (NIV) (night time NIV is permitted).
- Chronic use (daily intake >14 days), within one month of Day 1, of beta-2 agonists or any use of other bronchodilating medication (e.g., inhaled steroids, sympathomimetics, anticholinergics).
- Used carnitine, creatine, glutamine, oxatomide, idebenone or other forms of coenzyme Q10 or vitamin E or any other nutritional or antioxidant supplements or herbal medicines or anabolic steroids other than standard corticosteroids or puberty testosterone supplementation within 4 weeks of Day 1.
- Has an increased risk for opportunistic infections or systemic medical conditions resulting in significantly compromised immune system function

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

Duchenne UK

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