FibroGen - LELANTOS 2

A Phase 3 Trial of Pamrevlumab (FG-3019) or Placebo in Combination With Systemic Corticosteroids, in Ambulatory Subjects With Duchenne Muscular Dystrophy (DMD)

Hub Summary

This phase 3 study is looking at the efficacy and safety of pamrevlumab versus a placebo, in combination with corticosteroids (deflazacourt or prednisone). The trial is open to patients who are able to complete the 6 Minute Walk test (6MWD) with a distance of at least 270m but no more than 450m on two occasions 3 months before starting on the trial, as well as being able to rise from the floor (TTSTAND) in less than 10 seconds at the screening visit. Patients must also be on a stable dose of corticosteroids for a minimum of 6 months.

There will be a placebo arm of the trial and 50% of the patients will be randomly allocated to each arm. Once all patients have completed the 52-week study, they may be eligible for rollover into an open-label extension (OLE) with pamrevlumab + corticosteroids.

Pamrevlumab targets connective tissue growth factor (CFGF), which leads to muscle fibrosis. Stopping CTGF can improve muscle function. Data from the open-label Phase 2 clinical trial has shown that lung, heart and upper arm function was better preserved than usually expected in the normal progression of DMD.

Study Number: NCT04632940

Description by FibroGen

This is a global, randomized, double-blind, trial of pamrevlumab or placebo in combination with systemic corticosteroids in subjects with Duchenne muscular dystrophy, aged 6 to <12 years (ambulatory subjects only). Approximately 70 subjects will be randomized at a 1:1 ratio to Arm A (pamrevlumab + systemic deflazacort or equivalent potency of corticosteroids administered orally) or Arm B (placebo+ systemic deflazacort or equivalent potency of corticosteroids administered orally), respectively.

Subjects must be fully informed of the potential benefits of approved products and make an informed decision when participating in a clinical trial in which they could be randomized to placebo.

Subjects will be randomized in a 1:1 ratio to one of the two study treatment arms; pamrevlumab or placebo. Randomization will be stratified by exon 44 deletion.

The main study has three study periods:

- Screening period: Up to 4 weeks
- Treatment period: 52 weeks
- Safety Follow-up period/final assessment: A visit 28 days (+/- 3 Days) and a final safety follow-up phone call 60 days (+ 3 Days) after the last dose

Each subject will receive pamrevlumab or placebo at 35 mg/kg every 2 weeks for up to 52 weeks. Subjects who complete 52 weeks of treatment may be eligible for an open-label extension (OLE), offering extended treatment with pamrevlumab.

Subjects who discontinue study treatment for any reason should be encouraged to return to the investigative site to complete final safety and efficacy assessments.

Trial Status
Trial terminated

UK Locations
Leeds, Trial complete/terminated

Trial Sponsor
FibroGen

Age
6-12

Mutation Specific
Non-mutation specific therapies

Muscle Biopsy
No Muscle Biopsy Required

MRI
Yes

Phase
3

Length Of Participation
52 weeks

Recruitment Target
70

Ambulatory
Ambulant

dmdhub.org

Primary Outcome Measures

Ambulatory function assessment: [Time Frame: baseline to Week 52]

- Change in NorthStar Ambulatory Assessment (NSAA) Linearized total score

Secondary Outcome Measures

Other Muscle function assessments: [Time Frame: baseline to Week 52]

- Change in 4-stair climb Velocity (4SCV) assessment

Other Muscle function assessments: [Time Frame: baseline to Week 52]

- Change in the 10-meter walk/run test

Other Muscle function assessments: [Time Frame: baseline to Week 52]

- Changes in Time to Stand (TTSTAND)

Other Muscle function assessments: [Time Frame: baseline to Week 52]

- Time to Loss of Ambulation (LoA)

Can I take part?

Inclusion Criteria

Age, and consent:

- Males at least 6 to <12 years of age at screening initiation
- Written consent by legal guardian as per regional/ country and/or IRB/IEC requirements

DMD diagnosis:

- Medical history includes diagnosis of DMD and confirmed Duchenne mutation using a validated genetic test.

Pulmonary criteria:

- Average (of screening and day 0) percent predicted FVC above 45%

Corticosteroid treatment

- On a stable dose of systemic corticosteroids for a minimum of 6 months, with no substantial change in dosage for a minimum of 3 months (except for adjustments for changes in body weight) prior to screening. Corticosteroid dosage should be in compliance with the DMD Care Considerations Working Group recommendations (e.g. prednisone or prednisolone 0.75 mg/kg per day or deflazacort 0.9 mg/kg per day) or stable dose. A reasonable expectation is that dosage and dosing regimen would not change significantly for the duration of the study.

Performance criteria:

- Able to complete 6MWD test with a distance of at least 270M but no more than 450M on two occasions within 3 months prior to Randomization with ≤10% variation between these two tests.
- Able to rise (TTSTAND) from floor in <10 seconds (without aids/orthoses) at screening visit.
- Able to undergo MRI test for the lower extremities vastus lateralis muscle.

Vaccination:

- Received pneumococcal vaccine (PPSV23) (or any other pneumococcal polysaccharide vaccine as per national recommendations) and is receiving annual influenza vaccinations.

Laboratory criteria:

- Adequate renal function: cystatin C ≤1.4 mg/

- Adequate hematology and electrolytes parameters:

1. Platelets >100,000/mcL
2. Hemoglobin >12 g/dL
3. Absolute neutrophil count >1500 /µL
4. Serum calcium (Ca), potassium (K), sodium (Na), magnesium (Mg) and phosphorus (P) levels are within a clinically accepted range

Adequate hepatic function:

- No history or evidence of liver disease
- Gamma glutamyl transferase (GGT) ≤3x upper limit of normal (ULN)
- Total bilirubin ≤1.5xULN

Exclusion Criteria

- Concurrent illness other than DMD that can cause muscle weakness and/or impairment of motor function
- Severe intellectual impairment (eg, severe autism, severe cognitive impairment, severe behavioral disturbances) preventing the ability to perform study assessments in the Investigator's judgment
- Previous exposure to pamrevlumab
- BMI ≥40 kg/m2 or weight >117 kg
- History of allergic or anaphylactic reaction to human, humanized, chimeric or murine monoclonal antibodies
- Exposure to any investigational drug (for DMD or not), in the 30 days prior to screening initiation or use of approved DMD therapies (e.g., eteplirsen, ataluren, golodirsen) within 5 half-lives of screening, whichever is longer with the exception of the systemic corticosteroids, including deflazacort

Pulmonary and Cardiac criteria:

- Requires ≥16 hours continuous ventilation
- 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
- Hospitalization due to respiratory failure within the 8 weeks prior to screening
- Severe uncontrolled heart failure (NYHA Classes III-IV), including any of the following:
- Need for intravenous diuretics or inotropic support within 8 weeks prior to screening
- Hospitalization for a heart failure exacerbation or arrhythmia within 8 weeks prior to screening
- Arrhythmia requiring anti-arrhythmic therapy
- Any other evidence of clinically significant structural or functional heart abnormality

Clinical judgment:

- The Investigator judges that the subject will be unable to fully participate in the study and complete it for any reason, including inability to comply with study procedures and treatment, or any other relevant medical, surgical or psychiatric conditions

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

Duchenne UK