A Phase 3, Randomized, Double-Blind, Trial of Pamrevlumab (FG-3019) or Placebo in Combination with Systemic Corticosteroids in ambulatory subjects with Duchenne Muscular Dystrophy (DMD)

Published: 09-02-2021
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To evaluate the efficacy and safety of pamrevlumab versus placebo in combination with systemic corticosteroids administered every two weeks in ambulatory subjects with Duchenne muscular dystrophy (age 6 to

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Musculoskeletal and connective tissue disorders congenital
Study type	Interventional

Summary

ID

NL-OMON54230

Source
ToetsingOnline

Brief title
LELANTOS TWO

Condition

- Musculoskeletal and connective tissue disorders congenital
- Musculoskeletal and connective tissue disorders congenital

Synonym
Duchenne disease, Duchenne Muscular Dystrophy

Research involving
Human

Sponsors and support

Primary sponsor: FibroGen, Inc.
Source(s) of monetary or material Support: FibroGen;Inc.

Intervention

Keyword: Duchenne Muscular Dystrophy (DMD), Pamrevlumab, Phase 3, Placebo-controlled

Outcome measures

Primary outcome

Ambulatory functional assessment:

• Change in NorthStar Ambulatory Assessment (NSAA) total score from baseline to

Week 52.

Secondary outcome

Secondary Endpoints:

Other Muscle function assessments:

• Change in 4-stair climb Velocity (4SCV) assessment from baseline to Week 52.

• Change in the 10-meter walk/run test from baseline to Week 52.

• Changes in Time to Stand (TTSTAND) from baseline to Week 52.

• Time to Loss of Ambulation (LoA) from baseline to Week 52

Exploratory Endpoint:

• Change in Duchenne Video Assessment severity percentage from baseline to Week

52.

• Change in ppFVC and ppPEF assessed by spirometry, from baseline to Week 52.

MRI Assessment:

• Changes in lower extremities vastus lateralis muscle fibrosis score from baseline to Week 52, assessed by MRI.

Safety Assessments

• All treatment emergent adverse events (TEAEs), serious adverse events (SAEs), clinically significant laboratory test abnormalities, discontinuation of treatment due to treatment-related AEs and hypersensitivity/anaphylactic reactions.

• Number and percentage of subjects with hospitalizations due to any serious adverse events with pulmonary and/or cardiac cause(s).

• Number and percentage of subjects with bone fractures

• Annualized height velocity, HV (cm/year) from Baseline to Week 52

Pharmacokinetics/pharmacodynamics (PK/PD) assessment

• Population PK/PD analysis.

Study description

Background summary

See protocol section 2. Introduction

Study objective

To evaluate the efficacy and safety of pamrevlumab versus placebo in combination with systemic corticosteroids administered every two weeks in ambulatory subjects with Duchenne muscular dystrophy (age 6 to <12 years).

Study design

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 who complete 52 weeks of treatment may be eligible to enter into the open-label, extension treatment (OLE) with pamrevlumab + systemic corticosteroids

Intervention

The duration of total involvement in the study will be approximately 64 weeks (4 weeks in screening, 52 weeks of treatment, a follow-up visit 4 weeks later and a final follow-up phone call 60 days after the last dose). It may take up to 4 weeks to determine whether or not someone is able to participate in this study, based on meeting the inclusion/exclusion criteria. If he meets the inclusion criteria and decides to participate in this study, he will be randomly assigned to 1 of 2 treatment groups:
Treatment Group A: Pamrevlumab + systemic corticosteroid
Treatment Group B: Placebo + systemic corticosteroid
The study drug or placebo will be infused every 2 weeks for a total of 27 infusions over the 52 week Treatment Period. If he completes the full 52 week treatment period, he will be asked to return approximately 30 days after the last dose of study drug for a safety assessment. Approx. 60 days after the last dose of study drug follows an follow-up phone call.
If, eligible patient may partiicpate in the open label extention phase upon competion of Week 52 of the double blind phase.

Study burden and risks

PAMREVLUMAB RISKS
Pamrevlumab has been studied in adult patients with different diseases, such as lung disease, kidney disease in people with diabetes, liver scarring from hepatitis B infection, Duchenne Muscular Dystrophy (weakness of the muscles in children and young adults) and cancer of the pancreas.

To date the most common possible side effects experienced by patients treated with pamrevlumab in Duchenne Muscular Dystrophy
were:
• Headache
• Nasopharyngitis (inflammation of the nose, back of the mouth and throat)
• Vomiting
• Cough
• Fever (pyrexia)

• Back pain
• Nausea

Hypersensitivity reactions may develop in people taking pamrevlumab. On rare occasions, serious allergic reactions including anaphylaxis, have been observed in patients taking pamrevlumab and blinded study drug. These events occurred during study drug administration and responded to treatment. The following symptoms may be sign of an allergic reaction:
• A rash
• Have a hard time breathing
• Wheezing
• A sudden drop in blood pressure
• Swelling around the mouth, throat, or eyes
• A fast pulse
• Sweating more than usual

RISKS OF CORTICOSTEROIDS
The child is taking corticosteroids, which may have side effects for him. One of them is a too slow response to stress (due to illness or an infection).

OTHER RISKS
The patient's condition may not get better or may become worse during this study. Because of the way that pamrevlumab works, it is possible that wounds or fractures could heal more slowly or less completely due to taking pamrevlumab. Although this has not been seen in animal models of wound healing or human studies to date.
Interaction of pamrevlumab with other medications has not been studied. As with all drugs, the study drug may interact with other prescription drugs, non-prescription drugs, and supplements or herbal remedies.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Inclusion criteria

Subjects must meet all of the following criteria in order to be eligible for the study: Age, and consent: 1. Males at least 6 to <12 years of age at screening initiation 2. Written consent by patient and/legal guardian as per regional/ country and/or IRB/IEC requirements DMD diagnosis: 3. Medical history includes diagnosis of DMD and confirmed Duchenne mutation using a validated genetic test. Pulmonary criteria: 4. Average (of Screening and Day 0) percent predicted FVC above 45% 5. 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: 6. 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 :S10% variation between these two tests. 7. Able to rise (TTSTAND) from floor in <10 seconds (without aids/orthoses) at screening visit. 8. Able to undergo MRI test for the lower extremities vastus lateralis muscle. Vaccination: 9. Agreement to receive annual influenza vaccinations during the course of the study. Laboratory criteria: 10. Adequate renal function: cystatin C :S1.4 mg/L 11. Adequate hematology and electrolytes parameters: a. Platelets >100,000/mcL b. Hemoglobin >12 g/dL c. Absolute neutrophil count >1500 /µL d. Serum calcium (Ca), potassium (K), sodium (Na), magnesium (Mg) and phosphorus (P) levels are within a clinically accepted range for DMD patients 12. Adequate hepatic function: a. No history or evidence of liver disease b. Gamma glutamyl transferase (GGT) :S3x upper limit of normal (ULN) c. Total bilirubin :S1.5xULN

Exclusion criteria

Subjects must not meet any of the following criteria in order to be eligible: General Criteria: 1. Concurrent illness other than DMD that can cause muscle weakness and/or impairment of motor function 2. Severe intellectual impairment (eg, severe autism, severe cognitive impairment, severe behavioral disturbances) preventing the ability to perform study assessments in the Investigator*s judgment 3. Previous exposure to pamrevlumab 4. BMI

>40 kg/m2 or weight >117 kg 5. History of : a) allergic or anaphylactic reaction to human, humanized, chimeric or murine monoclonal antibodies b) hypersensitivity to study drug or any component of study drug 6. 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 (exondys 51), ataluren, golodirsen (vyondys 53), casimersen (amondys 45)) within 5 half-lives of screening, whichever is longer with the exception of the systemic corticosteroids, including deflazacort Pulmonary, Renal and Cardiac criteria: 7. Requires >=16 hours continuous ventilation 8. 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 9. Hospitalization due to respiratory failure within the 8 weeks prior to screening 10. Severe uncontrolled heart failure (NYHA Classes III-IV), or renal dysfunction, including any of the following: a. Need for intravenous diuretics or inotropic support within 8 weeks prior to screening b. Hospitalization for a heart failure exacerbation or arrhythmia within 8 weeks prior to screening c. Patients with glomerular filtration rate (GFR) of less than 30 ml/min/1,73 m^2 or with other evidence of acute kidney injury as determined by investigator 11. Arrhythmia requiring anti-arrhythmic therapy 12. Any other evidence of clinically significant structural or functional heart abnormality Clinical judgment: 13. 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

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-03-2022
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Pamrevlumab
Generic name:	Pamrevlumab

Ethics review

Approved WMO Date:	09-02-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-06-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-07-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-08-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-11-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-12-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-01-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	08-02-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-02-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-03-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-07-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-08-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2020-000699-39-NL

Register	ID
CCMO	NL76025.091.21