Domagrozumab phase 2 [TERMINATED]

Please note that Pfizer stopped the development of this drug after the Phase 2 failed to meet its primary endpoint.

Hub Summary

This phase 2 trial is designed to evaluate the safety and efficacy of Domagrozumaub, a myostatin inhibitor. Myostatin is a protein in the body which inhibits muscle growth and it is required to stop muscles from growing too large. It is thought that inhibiting myostatin may help preserve or improve muscle function in patients with DMD.

Study Number: NCT02310763

Description by Pfizer

This is a Phase 2 randomised, 2-period, double-blind, placebo-controlled, multiple ascending dose study to evaluate the safety, efficacy, pharmacokinetic (PK) and (pharmacodynamic) PD of PF-06252616 administered to ambulatory boys diagnosed with Duchenne Muscular Dystrophy. Three intravenous (IV) dose levels will be investigated in a within-subject dose-escalating fashion. Subjects will be randomly assigned to 1 of 3 sequence groups for approximately 96 weeks (2 periods of 48 weeks each). In period 1, two of the sequence groups will receive PF-06252616 and one sequence group will receive placebo. In period 2, the placebo group will switch to PF-06252616 and the two remaining sequence groups will either receive placebo or PF-06252616. Efficacy will be based on an observed mean change from baseline on function (4 stair climb) of PF-06252616 as compared to the placebo at the end of period 1. Period 2 provides an opportunity to evaluate PK. Subjects will receive monthly IV infused doses of either PF-06252616 or placebo and will undergo safety evaluations (Laboratory, cardiac monitoring, physical exams, x-ray, MRI), functional evaluations (pulmonary function testing, 4 stair climb, range of motion, strength testing, Northstar Ambulatory Assessment (NSAA) - upper limb functional testing (PUL) and the six-minute walk test (6MWDT), PK testing and PD testing to evaluate changes in muscle volume (MRI).

Primary Outcome Measures

- Incidence of dose-limiting or intolerability treatment-related AEs [Time Frame: Baseline through 49 Weeks]
- Mean change from baseline on the 4 Stair Climb (4SC) as compared to placebo in seconds [Time Frame: Baseline, 49 Weeks]

Secondary Outcome Measures

- Mean change from baseline as compared to placebo of Forced Vital Capacity in litres [Time Frame: Baseline, 17, 33 and 49 Weeks]
- Mean change from baseline as compared to placebo in the NSAA score [Time Frame: Baseline, 17, 33 and 49 Weeks]
- Mean change from baseline as compared to placebo in the ankle range of motion [Time Frame: Baseline, 17, 33 and 49 Weeks]
- Mean change from baseline as compared to placebo in the PUL score [Time Frame: Baseline, 17, 33 and 49 Weeks]
- Mean change from baseline as compared to placebo in the 6MWD in meters [Time Frame: Baseline, 17, 33 and 49 Weeks]
- Mean change from baseline as compared to placebo muscle strength as measured by hand held myometry [Time Frame: Baseline, 17, 33 and 49 Weeks]
- Mean change from baseline as compared to placebo in the thigh muscle volume by MRI [Time Frame: Baseline, 17, 33 and 49 Weeks]
- Area Under the Curve from Time Zero to end of dosing interval (AUCtau) of GDF-8 [Time Frame: Baseline through 93 Weeks]

Trial Status
Trial terminated

UK Locations

Trial Sponsor
Pfizer

Age
6-16

Mutation Specific
Non-mutation specific therapies

Muscle Biopsy
No Muscle Biopsy Required

MRI
Yes

Phase
2

Length Of Participation
96 weeks

Recruitment Target
121

Ambulatory
Ambulant

Therapeutic Category
Myostatin inhibitor

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- Immunogenicity: Incidence of anti-drug antibody [Time Frame: Baseline through 97 Weeks]

Can I take part?

Inclusion Criteria

- Ambulatory boys age 6 to <16 years old (at the time of randomization), diagnosed with DMD. Diagnosis must be confirmed in subject's medical history and by genetic testing obtained during routine clinical care for diagnostic purposes as reported from an appropriate regulated laboratory using a clinically validated genetic test (genetic testing is not provided by the sponsor).
- Subjects who are able to perform the 4-stair climb in > or = 0.33 but < or =1.6 stairs/second.
- Subjects must be receiving glucocorticosteroids for a minimum of 6 months prior to signing informed consent. There should be no significant change (>0.2 mg/kg) in dosage or dose regimen (not related to body weight change) for at least 3 months immediately prior to signing the informed consent and a reasonable expectation that dosage and dosing regimen will not change significantly for the duration of the study.
- Adequate hepatic and renal function on screening laboratory assessments.
- No underlying disposition for iron accumulation on screening laboratory assessments.
- Iron content estimate on the screening liver MRI is within the normal range.

Exclusion Criteria

- Subjects with known cognitive impairment or behavioural issues that would impede the ability to follow instructions.
- History of major surgical procedure within 6 weeks of signing the informed consent or planned surgery during the study.
- Any injury which may impact functional testing. Previous injuries must be fully healed prior to consenting. Prior lower limb fractures must be fully healed and at least 3 months from injury date.
- Presence or history of other musculoskeletal or neurologic disease or somatic disorder not related to DMD including pulmonary and cardiac disease.
- Compromised cardiac function (left ventricular ejection fraction <55% as determined on a screening cardiac MRI or echocardiogram). Subjects may be receiving ACE (angiotensin converting enzyme) inhibitors or beta blockers, ARB (angiotensin II receptor antagonist) or aldosterone blocker/thiazide diuretic; however they must have initiated treatment more than 3 months prior to screening to ensure stable therapy.
- Evidence or history of clinically significant haematological, renal, endocrine, pulmonary, gastrointestinal, cardiovascular (including uncontrolled hypertension), hepatic, neurologic, or allergic disease (including drug allergies, but excluding untreated, asymptomatic, seasonal allergies at time of dosing).
- Documented history of iron overload including hemochromatosis, beta thalassemia major, beta thalassemia intermedia or hemolytic anaemia.
- Unwilling or unable (eg, metal implants, requires sedation) to undergo examination with closed MRI without sedation.
- Participation in other studies involving investigational drug(s) for a minimum of 30 days or within 5 half-lives (whichever is longer) prior to signing the informed consent and/or during study participation.
- Current or prior treatment with anti-myostatin, exon skipping, nonsense mutation-targeted therapies ever or more than 30 days of treatment with utrophin modifiers and treatment with utrophin modifiers within 30 days prior to signing the informed consent and/or during study participation.
- Current or prior treatment within the past 3 months with androgens or human growth hormone.
- Current treatment with immunosuppressant therapies (other than glucocorticoid steroids), aminoglycosides (eg, gentamicin), multivitamins with iron and iron supplements and other investigational therapies (including idebenone).

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

Duchenne UK

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