Sarepta - ESSENCE

A Double-Blind, Placebo-Controlled, Multi-Center Study With an Open-Label Extension to Evaluate the Efficacy and Safety of SRP-4045 and SRP-4053 in Patients With Duchenne Muscular Dystrophy

Summary

The main objective of this study is to evaluate the efficacy of SRP-4045 and SRP-4053 compared to placebo in Duchenne muscular dystrophy (DMD) patients with out-of-frame deletion mutations amenable to skipping exon 45 and exon 53, respectively. Part 1 is double-blind and randomised; Part 2 is open-label.

Study Number: NCT02500381

Description by Sarepta Therapeutics

This is a double-blind, placebo-controlled, multi-center study to evaluate the efficacy and safety of SRP-4045 and SRP-4053. Eligible patients with out-of-frame deletion mutations amenable to exon 45 or 53 skipping will be randomized to receive once weekly intravenous (IV) infusions of 30 mg/kg SRP-4045 or 30 mg/kg SRP-4053 respectively (combined-active group) or placebo for up to 96 weeks (the placebo-controlled period of the trial). This will be followed by an open label extension period in which all patients will receive open-label active treatment for 48 weeks (up to Week 144 of study).

The study will enrol approximately 222 patients, with a planned minimum target of 111 patients amenable to exon 45 skipping and 111 patients amenable to exon 53 skipping.

Approximately 148 patients will be randomized to receive active treatment with either SRP-4045 or SRP-4053 (depending on deletion mutation), and 74 patients will be randomized to receive placebo. Twice as many patients will receive active treatment as will receive placebo (2:1 randomization).

Clinical efficacy will be assessed at regularly scheduled study visits, including functional tests such as the six-minute walk test (6MWT). All patients will undergo a muscle biopsy at baseline and a second muscle biopsy either at Week 48 or Week 96.

Safety will be assessed through the collection of adverse events (AEs), laboratory tests, electrocardiograms (ECGs), echocardiograms (ECHOs), vital signs, and physical examinations throughout the study.

Blood samples will be taken periodically throughout the study to assess the pharmacokinetics of both drugs.

Primary Outcome Measures

- Change From Baseline in the Total Distance Walked During 6-Minute Walk Test (6MWT) at Week 96 [Time Frame: Baseline and Week 96]

Secondary Outcome Measures

- Change from Baseline the Total Distance Walked During 6-Minute Walk Test (6MWT) at Week 144 (Week 48 of the OL period) [Time Frame: Baseline, Week 144]
- Change from Baseline in Dystrophin Protein Levels Determined by Western Blot at Weeks 48 or 96 [Time Frame: Baseline and Weeks 48 or 96]
- Change from Baseline in Dystrophin Intensity Levels Determined by Immunohistochemistry (IHC) at Weeks 48 or 96 [Time Frame: Baseline and Weeks 48 or 96]
- Ability to Rise Independently From the Floor [Time Frame: Week 96, Week 144]
- Time to Loss of Ambulation (LOA) [Time Frame: Baseline, Week 96, Week 144]
- Change From Baseline in the North Star Ambulatory Assessment (NSAA) Total Score at Week 96 and Week 144 [Time Frame: Baseline, Week 96, Week 144]
- Change From Baseline in Forced Vital Capacity Percent (FVC%) Predicted at Week 96 and Week 144 [Time Frame: Baseline, Week 96, Week 144]

Can I take part?

Inclusion Criteria

- Males between 7 and 13 years of age, inclusive.
- Have a clinical diagnosis of Duchenne Muscular Dystrophy, and an out-of-frame deletion amenable to exon 45 or exon 53 skipping.
- Have stable pulmonary function (FVC % of predicted greater than or equal to (≥) 50%, and no requirement for night time ventilation).
- Have intact left and right biceps, or 2 alternative upper arm muscle groups.
- Have been on a stable dose of corticosteroids for at least 24 weeks (6 months).
- Average 6-minute walk test (6MWT) distance of greater than or equal to (≥) 300 metres, and less than or equal to (≤) 450 metres.

Exclusion Criteria

- Previous treatment at any time which involved gene therapy, cell-based therapy (eg, stem cell transplantation), nucleic acid antisense therapy.
- Previous treatment within the last 24 weeks (6 months) with valmorolone, PRO045, PRO053, anti-fibrotic or anti-inflammatory agents.
- Previous treatment within the last 12 weeks (3 months) with metformin, sildenafil, and other nitric oxide (NO)-active agents.
- Current or previous treatment with any other experimental treatment (other than deflazacort) within 12

AUSNMD

Trial Status
Recruiting

Locations
Brisbane - Queensland Children's Hospital, Recruiting, Melbourne - Melbourne Children's Campus, Recruiting, Sydney - Westmead Children's Hospital, Recruiting

Trial Sponsor
Sarepta Therapeutics

Age
7-13

Mutation Specific
Yes, Must be amenable to exon 45 or exon 53 skipping

Muscle Biopsy
Yes

MRI
No

Phase
3

Length Of Participation
Up to 96 weeks (double-blind period)

Recruitment Target
222

Ambulatory
Yes

weeks prior to Week 1.

- Participation in any other DMD interventional clinical study within 12 weeks prior to Week 1.
- Major surgery within 3 months prior to Week 1.
- Presence of any other clinically significant illness.

Other inclusion/exclusion criteria apply.

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

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Therapeutic Category

Exon skipping