Sarepta- ESSENCE

Study of SRP-4045 and SRP-4053 in DMD Patients

Hub Summary

This study is a stage 3 trial of Sarepta's exon 45 and exon 53 skipping drugs. Exon skipping drugs use a small piece of genetic material to skip over the part of the dystrophin gene with a mutation. The part of the dystrophin gene with a mutation varies between patients. Therefore, exon skipping trials are mutation specific. This trial requires you to be amenable to the skipping of exon 45 or 53.

The main objective of this study is to determine the efficacy of the drugs compared to a placebo in DMD patients.

Study Number: NCT02500381

Description by Sarepta Therapeutics, Inc.

This is a double-blind, placebo-controlled, multi-centre 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, 84 patients) or placebo (43 patients) 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 up to 96 weeks.

The study will enrol approximately 126 patients, with a planned minimum target of 45 patients amenable to exon 45 skipping and 45 patients amenable to exon 53 skipping.

Approximately 66 patients will be randomized to receive active treatment with either SRP-4045 or SRP-4053 (depending on deletion mutation), and 33 patients will be randomized to receive placebo. Twice as many patients will receive active treatment as will receive placebo (2:1 randomization).

When approximately 75% of patients have been in the trial for 48 weeks a group of independent experts will review key study results and will make a determination on whether patients will roll into the open-label period of the study and receive active drug or continue in the placebo-controlled period out to Week 96 as planned.

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. All patients will undergo a second muscle biopsy 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 in 6 Minute Walk Test (6MWT) from Baseline [Time Frame: Baseline to Week 96]

Secondary Outcome Measures

- Dystrophin protein expression [Time Frame: Baseline to Week 48 pr Week 96]
- Ability to rise independently from the floor [Time Frame: Baseline to Week 96]
- Functional status as measured by loss of ambulation (LOA) from Baseline [Time Frame: Baseline to Week 96]
- North Star Ambulatory Assessment (NSAA) from Baseline [Time Frame: Baseline to Week 96]
- Forced vital capacity (FVC)% predicted from Baseline [Time Frame: Baseline to Week 96]
- Frequency of falls from Baseline [Time Frame: Baseline to Week 96]
- Left ventricular ejection fraction (LVEF) from baseline [Time Frame: Baseline to

Trial Status
Fully recruited

UK Locations
London - GOSH, Fully recruited, Alder Hey, Fully recruited, Glasgow, Fully recruited, Leeds, Fully recruited, Newcastle, Fully recruited, Oxford, Fully recruited, Temple Street, Fully recruited

Trial Sponsor
Sarepta Therapeutics, Inc.

Age
7-13

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

Muscle Biopsy
Muscle Biopsy Required

MRI
No

Phase
3

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

Recruitment Target
126

Ambulatory
Ambulant, 6MWT required

Therapeutic Category
Exon skipping

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Week 96]

- Intensity of dystrophin expression [Baseline to Week 49 or 96]

Can I take part?

Inclusion Criteria

- Stable dose of corticosteroids for 6 months+
- Intact right and left biceps or 2 alternative upper muscle groups
- Mean 6MWT greater than or equal to 300m and less than or equal to 450m.
- Stable pulmonary and cardiac function.

Exclusion Criteria

- Previous treatment with SMT C1100 (BMN-195) at any time
- Previous treatment with PRO045 or PRO053 within 6 months prior to week 1
- Current or previous treatment with any other experimental treatment (other than deflazacort) within 12 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 week1
- Presence of any other clinically significant illness.

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

Duchenne UK

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