A Randomized, Double-Blind, Dose Finding and Comparison Study of the Safety and Efficacy of High Doses of Eteplirsen, Preceded by an Open-Label Dose Escalation, in Patients with Duchenne Muscular Dystrophy With Deletion Mutations Amenable to Exon 51 Skipping

Published: 06-04-2020
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This study has been transitioned to CTIS with ID 2024-511492-15-00 check the CTIS register for the current data. Part 1:to evaluate the safety and tolerability of 2 doses (100 milligrams/kilogram [mg/kg] and 200 mg/kg) of eteplirsen in approximately...

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

Summary

ID

NL-OMON52516

Source
ToetsingOnline

Brief title
MIS51ON

Condition

- Musculoskeletal and connective tissue disorders congenital

Synonym
DMD, muscular dystrophy

Research involving
Human

Sponsors and support

Primary sponsor: Sarepta Therapeutics, Inc.
Source(s) of monetary or material Support: Sarepta Therapeutics

Intervention

Keyword: Duchenne Muscular Dystrophy, Eteplirsen

Outcome measures

Primary outcome

Part 1: Incidence of Adverse Events (AEs)

Time Frame: Up to Week 148

Part 2: Change From Baseline in the NSAA Total Score at Week 144

Time Frame: Baseline, Week 144

Secondary outcome

Part 2: Change From Baseline in Time to Rise From the Floor, Time to Complete

10-Meter Walk/Run, and the Timed Stair Ascend Test Baseline.

Time Frame: Baseline, Week 144

Part 2: Change From Baseline in the Total Distance Walked During 6-Minute Walk

Test (6MWT)

Time Frame: Baseline, Week 144

Part 2: Change from Baseline in Forced Vital Capacity Percent Predicted (FVC%p)

at Week 144

Time Frame: Baseline, Week 144

Part 2: Time to Loss of Ambulation (LOA)

Time Frame: Baseline up to Week 144

Part 2: Change From Baseline in Skeletal Muscle Dystrophin Expression

Time Frame: Baseline, Postdose (at Week 24, Week 48, or Week 144)

Part 2: Incidence of Adverse Events (AEs)

Time Frame: Baseline up to Week 148

Part 2: Pharmacokinetic (PK) Plasma Concentration of Eteplirsen

Time Frame: 0 (predose) to 2 hours postdose up to Week 144

Study description

Background summary

This study will be comprised of 2 parts: Part 1 (dose escalation) will be conducted to evaluate the safety and tolerability of 2 doses (100 milligrams/kilogram [mg/kg] and 200 mg/kg) of eteplirsen in approximately 10 participants with DMD; Part 2 (dose finding and dose comparison) will be conducted for the evaluation of high doses (100 mg/kg and 200 mg/kg) and its comparison with the 30 mg/kg dose of eteplirsen, in approximately 144 participants with genetically confirmed deletion mutations amenable to treatment by skipping exon 51.

Study objective

This study has been transitioned to CTIS with ID 2024-511492-15-00 check the CTIS register for the current data.

Part 1:to evaluate the safety and tolerability of 2 doses (100 milligrams/kilogram [mg/kg] and 200 mg/kg) of eteplirsen in approximately 10 participants with DMD;

Part 2 (dose finding and dose comparison) will be conducted for the evaluation of high doses (100 mg/kg and 200 mg/kg) and its comparison with the 30 mg/kg dose of eteplirsen, in approximately 144 participants with genetically confirmed deletion mutations amenable to treatment by skipping exon 51.

Study design

Design Details
Primary Purpose : Treatment
Allocation : Randomized
Interventional Model : Parallel Assignment
Masking : Quadruple (ParticipantCare ProviderInvestigatorOutcomes Assessor)
Masking Description: Part 1 is open-label, dose escalation; Part 2 is double-blind, dose finding, and dose comparison Arms and Interventions

Participant Group/Arm:

- Experimental: Part 1: Eteplirsen
Participants will receive eteplirsen 100 mg/kg once weekly for at least 4 weeks, followed by eteplirsen 200 mg/kg once weekly for at least 4 weeks.

- Active Comparator: Part 2: Eteplirsen 30 mg/kg
Randomized participants will receive eteplirsen 30 mg/kg once weekly for up to 144 weeks.

- Experimental: Part 2: Eteplirsen 100 mg/kg
Randomized participants will receive eteplirsen 100 mg/kg once weekly before the evaluation of the high doses occurs and then will receive the selected high dose once weekly for up to 144 weeks.

- Experimental: Part 2: Eteplirsen 200 mg/kg
Randomized participants will receive eteplirsen 200 mg/kg once weekly before the evaluation of the high doses occurs and then will receive the selected high dose once weekly for up to 144 weeks.

Intervention

Drug: Eteplirsen
• Solution for intravenous (IV) infusion.

• Other Names:
• AVI-4658
• EXONDYS 51
• EXONDYS

Study burden and risks

Please refer for the procedures to the protocol tables 2-8 Schedule of events (pages 8-23) or question E4.
The Possible side effects that are already known are described in the IB, patient information letter and question E9.

Contacts

Public
Sarepta Therapeutics, Inc.

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US
Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Children (2-11 years)

Inclusion criteria

Inclusion Criteria:
• Be a male with an established clinical diagnosis of DMD and an out-of-frame deletion mutation of the DMD gene amenable to exon 51 skipping.
• Ambulatory participant, able to perform TTRISE in 10 seconds or less at the time of screening visit.
• Able to walk independently without assistive devices.
• Have intact right and left biceps muscles or an alternative upper arm muscle group.
• Have been on a stable dose or dose equivalent of oral corticosteroids for at least 12 weeks prior to randomization and the dose is expected to remain constant (except for modifications to accommodate changes in weight and stress-related needs as per the recently published guidelines throughout the study.
• For ages 7 years and older, has stable pulmonary function (forced vital capacity >=50 percent (%) of predicted and no requirement for nocturnal ventilation). For ages 4 to 6 years, does not require support from ventilator or non-invasive ventilation at time of screening.

Exclusion criteria

Exclusion Criteria:
• Use of any pharmacologic treatment (other than corticosteroids) within 12 weeks prior to randomization.
• Current or previous treatment with any other experimental pharmacologic treatment for DMD or any prior exposure to antisense oligonucleotide, gene therapy or gene editing; except the following: Ezutromid in the last 12 weeks prior to first dose; Drisapersen in the last 36 weeks prior to first dose; Suvodirsen in the last 12 weeks prior to first dose; Vamorolone in the last 12 weeks prior to first dose; and Eteplirsen (previous or current use).
• Major surgery within 3 months prior to randomization.
• Presence of any other significant neuromuscular or genetic disease other than DMD.
• Presence of any known impairment of renal function and/or other clinically significant illness.
• Has evidence of cardiomyopathy, as defined by left ventricular ejection fraction less than <50% on the screening echocardiogram or Fridericia's correction formula (QTcF) >=450 millisecond based on the screening electrocardiograms (ECGs).
Other inclusion/exclusion criteria apply.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	19-01-2023
Enrollment:	1
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	06-04-2020
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-07-2020
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO	

Date:	03-08-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	30-09-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-12-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	23-12-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-12-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	25-03-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	03-06-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-07-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

	Haag)
Approved WMO Date:	26-08-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	30-08-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-09-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	03-11-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-11-2022
Application type:	Amendment
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Approved WMO Date:	22-12-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-12-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-01-2024

Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-03-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-05-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-06-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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
EU-CTR	CTIS2024-511492-15-00
EudraCT	EUCTR2018-001762-42-NL
ClinicalTrials.gov	NCT03992430
CCMO	NL70639.000.20