



Clinical trial results:

An Open-Label Safety, Tolerability, and Pharmacokinetics Study of Eteplirsen in Young Patients with Duchenne Muscular Dystrophy Amenable to Exon 51 Skipping

Summary

EudraCT number	2016-000951-29
Trial protocol	GB BE DE FR IT
Global end of trial date	10 March 2021

Results information

Result version number	v1 (current)
This version publication date	25 September 2021
First version publication date	25 September 2021

Trial information

Trial identification

Sponsor protocol code	4658-102
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03218995
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sarepta Therapeutics, Inc.
Sponsor organisation address	215 First Street, Cambridge, United States, 02142
Public contact	Medical Director, Sarepta Therapeutics, Inc., 1 800-690-2003, clinicaltrials@sarepta.com
Scientific contact	Medical Director, Sarepta Therapeutics, Inc., 1 800-690-2003, clinicaltrials@sarepta.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-001722-PIP01-14
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 May 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 March 2021
Global end of trial reached?	Yes
Global end of trial date	10 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The overall purpose of the study was to evaluate the safety and tolerability of eteplirsen in participants with Duchenne muscular dystrophy (DMD) aged 6 to 48 months.

Protection of trial subjects:

This study was conducted in accordance with the final study protocol and its amendments, Sponsor procedures, which comply with the ethical principles of Good Clinical Practice (GCP), and the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 August 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Belgium: 2
Worldwide total number of subjects	15
EEA total number of subjects	9

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	6
Children (2-11 years)	9
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0
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Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants with genotypically confirmed Duchenne muscular dystrophy (DMD) featuring a deletion mutation amenable to exon 51 skipping were enrolled into 2 cohorts based on their age.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Eteplirsen
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Arm description:

Eteplirsen was administered once every 7 days by intravenous (IV) infusion starting on Day 1 for up to 96 weeks. The starting dose was 2 milligrams/kilogram (mg/kg) eteplirsen, with escalation to 4, 10, 20, and 30 mg/kg for 10 weeks, and then participants continued to receive eteplirsen at 30 mg/kg for the duration of the study.

Arm type	Experimental
Investigational medicinal product name	Eteplirsen
Investigational medicinal product code	
Other name	AVI-4658; EXONDYS 51®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eteplirsen was administered per schedule specified in the arm description.

Number of subjects in period 1	Eteplirsen
Started	15
Received at least 1 dose of study drug	15
Completed	15

Baseline characteristics

Reporting groups

Reporting group title	Overall Study
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Reporting group description:

Eteplirsen was administered once every 7 days by IV infusion starting on Day 1 for up to 96 weeks. The starting dose was 2 mg/kg eteplirsen, with escalation to 4, 10, 20, and 30 mg/kg for 10 weeks, and then participants continued to receive eteplirsen at 30 mg/kg for the duration of the study.

Reporting group values	Overall Study	Total	
Number of subjects	15	15	
Age Categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	6	6	
Children (2-11 years)	9	9	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: months			
arithmetic mean	28.5		
standard deviation	± 12.94	-	
Gender Categorical			
Units: Subjects			
Female	0	0	
Male	15	15	
Race			
Race data are reported as "Missing" for participants from France because French sites and the French Regulations prohibit the entry of race and ethnicity.			
Units: Subjects			
White	9	9	
Other	1	1	
Missing	5	5	
Ethnicity			
Ethnicity data are reported as "Missing" for participants from France because French sites and the French Regulations prohibit the entry of race and ethnicity.			
Units: Subjects			
Not Hispanic or Latino	7	7	
Not reported	2	2	
Unknown	1	1	
Missing	5	5	

Subject analysis sets

Subject analysis set title	Cohort 1: Age 24 to 48 Months
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants aged 24 to 48 months old were administered eteplirsen once every 7 days by IV infusion starting on Day 1 for up to 96 weeks. The starting dose was 2 mg/kg eteplirsen, with escalation to 4, 10, 20, and 30 mg/kg for 10 weeks, and then participants continued to receive eteplirsen at 30 mg/kg for the duration of the study.

Subject analysis set title	Cohort 2: Age 6 to <24 Months
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants aged 6 to <24 months old were administered eteplirsen once every 7 days by IV infusion starting on Day 1 for up to 96 weeks. The starting dose was 2 mg/kg eteplirsen, with escalation to 4, 10, 20, and 30 mg/kg for 10 weeks, and then participants continued to receive eteplirsen at 30 mg/kg for the duration of the study.

Reporting group values	Cohort 1: Age 24 to 48 Months	Cohort 2: Age 6 to <24 Months	
Number of subjects	9	6	
Age Categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	6	
Children (2-11 years)	9	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: months			
arithmetic mean	36.8	16.0	
standard deviation	± 8.21	± 7.07	
Gender Categorical Units: Subjects			
Female	0	0	
Male	9	6	
Race			
Race data are reported as "Missing" for participants from France because French sites and the French Regulations prohibit the entry of race and ethnicity.			
Units: Subjects			
White	6	3	
Other	0	1	
Missing	3	2	
Ethnicity			
Ethnicity data are reported as "Missing" for participants from France because French sites and the French Regulations prohibit the entry of race and ethnicity.			
Units: Subjects			
Not Hispanic or Latino	4	3	
Not reported	2	0	
Unknown	0	1	
Missing	3	2	

End points

End points reporting groups

Reporting group title	Eteplirsen
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Reporting group description:

Eteplirsen was administered once every 7 days by intravenous (IV) infusion starting on Day 1 for up to 96 weeks. The starting dose was 2 milligrams/kilogram (mg/kg) eteplirsen, with escalation to 4, 10, 20, and 30 mg/kg for 10 weeks, and then participants continued to receive eteplirsen at 30 mg/kg for the duration of the study.

Subject analysis set title	Cohort 1: Age 24 to 48 Months
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants aged 24 to 48 months old were administered eteplirsen once every 7 days by IV infusion starting on Day 1 for up to 96 weeks. The starting dose was 2 mg/kg eteplirsen, with escalation to 4, 10, 20, and 30 mg/kg for 10 weeks, and then participants continued to receive eteplirsen at 30 mg/kg for the duration of the study.

Subject analysis set title	Cohort 2: Age 6 to <24 Months
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants aged 6 to <24 months old were administered eteplirsen once every 7 days by IV infusion starting on Day 1 for up to 96 weeks. The starting dose was 2 mg/kg eteplirsen, with escalation to 4, 10, 20, and 30 mg/kg for 10 weeks, and then participants continued to receive eteplirsen at 30 mg/kg for the duration of the study.

Primary: Number of Participants with Treatment Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), and TEAEs Leading to Discontinuation from Study Drug

End point title	Number of Participants with Treatment Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), and TEAEs Leading to Discontinuation from Study Drug ^[1]
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End point description:

TEAEs were defined as adverse events (AEs) with an onset following administration of the first dose of study drug. An AE was any untoward medical occurrence in a participant, which does not necessarily have a causal relationship with the study drug. Abnormalities presented at Baseline were considered AEs if they reoccurred after resolution or worsened during the AE collection period. An SAE was defined as any AE that, in the view of either the Investigator or Sponsor, resulted in any of the following outcomes as fatal, life-threatening, required hospitalization or prolongation of existing hospitalization, persistent or significant disability/incapacity, a congenital anomaly/birth defect, or an important medical event. A summary of all SAEs and Other AEs (nonserious) regardless of causality is located in the 'Adverse Events' Section. The Safety Set included all participants who were enrolled and received at least 1 dose of eteplirsen during the study.

End point type	Primary
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End point timeframe:

Baseline up to Week 100

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Analysis were descriptive in nature.

End point values	Cohort 1: Age 24 to 48 Months	Cohort 2: Age 6 to <24 Months		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	6		
Units: participants				
TEAE	9	6		
SAE	0	1		

AE leading to discontinuation from study drug	0	0		
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Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with at Least 1 Potentially Clinically Significant Clinical Safety Laboratory Abnormality

End point title	Number of Participants with at Least 1 Potentially Clinically Significant Clinical Safety Laboratory Abnormality ^[2]
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End point description:

Clinical laboratory parameters that were evaluated included

- Any Grade ≥ 2 (moderate) or serious event without an alternative etiology that the Investigator deemed was related to study drug
- Two consecutive drug-related serum creatinine levels $\geq 2 \times$ upper limit of normal (ULN) without an alternative etiology
- Creatine kinase (CK) levels $> 50,000$ units/liter (U/L)
- A confirmed, unexplained, increase in gamma glutamyl transferase (GGT) $> 3 \times$ ULN and either an increase in bilirubin $> 2 \times$ ULN or nascent prothrombin time $> 2 \times$ ULN concurrently, without an alternative etiology

End point type	Primary
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End point timeframe:

Baseline up to Week 100

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Analysis were descriptive in nature.

End point values	Cohort 1: Age 24 to 48 Months	Cohort 2: Age 6 to <24 Months		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	6		
Units: participants	9	6		

Statistical analyses

No statistical analyses for this end point

Primary: Abnormal Changes from Baseline or Worsening of Physical Examination Findings

End point title	Abnormal Changes from Baseline or Worsening of Physical Examination Findings ^[3]
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End point description:

Data not collected during the study for this Outcome Measure. A summary of all SAEs and Other AEs (nonserious) regardless of causality is located in the 'Adverse Events' Section.

End point type	Primary
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End point timeframe:

Baseline up to Week 100

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Analysis were descriptive in nature.

End point values	Cohort 1: Age 24 to 48 Months	Cohort 2: Age 6 to <24 Months		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0 ^[4]	0 ^[5]		
Units: Not applicable				
number (not applicable)				

Notes:

[4] - Data not collected.

[5] - Data not collected.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with at Least 1 Markedly Abnormal Vital Sign

End point title	Number of Participants with at Least 1 Markedly Abnormal Vital Sign ^[6]
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End point description:

The vital sign parameters that were evaluated included blood pressure, heart rate, respiration, and temperature. A summary of all SAEs and Other AEs (nonserious) regardless of causality is located in the 'Adverse Events' Section. The Safety Set included all participants who were enrolled and received at least 1 dose of eteplirsen during the study.

End point type	Primary
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End point timeframe:

Baseline up to Week 100

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Analysis were descriptive in nature.

End point values	Cohort 1: Age 24 to 48 Months	Cohort 2: Age 6 to <24 Months		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	6		
Units: participants	9	6		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with at Least 1 Markedly Abnormal Electrocardiogram (ECG) and Echocardiogram (ECHO)

End point title	Number of Participants with at Least 1 Markedly Abnormal Electrocardiogram (ECG) and Echocardiogram (ECHO) ^[7]
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End point description:

The ECG was manually reviewed and interpreted by medically qualified personnel using a central vendor

according to pre-specified criteria. The Investigator determined if the findings in the centrally read ECG report were clinically significant. Clinical significance was defined as any variation in ECG findings that had medical relevance resulting in an alteration in medical care. The ECHO was reviewed and interpreted by medically qualified personnel using a central vendor according to pre-specified criteria. The Investigator determined if the findings in the ECHO report were clinically significant. Clinical significance was defined as any variation in ECHO findings that had medical relevance resulting in an alteration in medical care. A summary of all SAEs and Other AEs (nonserious) regardless of causality is located in the 'Adverse Events' Section. The Safety Set included all participants who were enrolled and received at least 1 dose of eteplirsen during the study.

End point type	Primary
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End point timeframe:

Weeks 8, 12, 24, 36, 48, 60, 72, 84, 96

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Analysis were descriptive in nature.

End point values	Cohort 1: Age 24 to 48 Months	Cohort 2: Age 6 to <24 Months		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	6		
Units: participants	4	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (Cmax) of Eteplirsen

End point title	Maximum Plasma Concentration (Cmax) of Eteplirsen
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End point description:

The Safety Set was used for pharmacokinetic(s) (PK) analysis and included all participants who were enrolled and received at least 1 dose of eteplirsen during the study. PK data were not collected for participants who received 4 mg of eteplirsen. Here, 'n' signifies number of participants evaluable at the specified timepoint.

End point type	Secondary
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End point timeframe:

Pre-infusion, immediately prior to end of infusion, and approximately 1-3 hours and 6-8 hours after completion of infusion during Weeks 2 (2 mg/kg dose level), 6 (10 mg/kg dose level), 8 (20 mg/kg dose level), and 10 and 24 (30 mg/kg dose level)

End point values	Cohort 1: Age 24 to 48 Months	Cohort 2: Age 6 to <24 Months		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	6		
Units: microgram per milliliter (µg/mL)				
geometric mean (geometric coefficient of variation)				
Week 2 (2 mg/kg [n=8, 5])	9.67 (± 75.9)	4.22 (± 120)		
Week 6 (10 mg/kg)	46.5 (± 72.3)	17.2 (± 192)		
Week 8 (20 mg/kg)	63.3 (± 123)	85.0 (± 67.6)		

Week 10 (30 mg/kg)	93.7 (± 55.5)	63.8 (± 124)		
Week 24 (30 mg/kg [n=8, 6])	78.2 (± 92.2)	59.7 (± 82.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Plasma Concentration (Tmax) of Eteplirsén

End point title	Time to Reach Maximum Plasma Concentration (Tmax) of Eteplirsén
End point description: The Safety Set was used for PK analysis and included all participants who were enrolled and received at least 1 dose of eteplirsén during the study. PK data were not collected for participants who received 4 mg of eteplirsén. Here, 'n' signifies number of participants evaluable at the specified timepoint.	
End point type	Secondary
End point timeframe: Pre-infusion, immediately prior to end of infusion, and approximately 1-3 hours and 6-8 hours after completion of infusion during Weeks 2 (2 mg/kg dose level), 6 (10 mg/kg dose level), 8 (20 mg/kg dose level), and 10 and 24 (30 mg/kg dose level)	

End point values	Cohort 1: Age 24 to 48 Months	Cohort 2: Age 6 to <24 Months		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	6		
Units: hours (hr)				
median (full range (min-max))				
2 mg/kg (Week 2 [n= 8, 5])	0.58 (0.17 to 2.67)	0.58 (0.42 to 0.67)		
10 mg/kg (Week 6)	0.58 (0.47 to 4.25)	0.72 (0.58 to 3.32)		
20 mg/kg (Week 8)	0.78 (0.50 to 2.75)	0.73 (0.53 to 1.17)		
30 mg/kg (Week 10)	0.58 (0.50 to 1.48)	0.92 (0.50 to 2.75)		
30 mg/kg (Week 24 [n=8, 6])	0.63 (0.42 to 6.83)	0.72 (0.58 to 1.83)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under Concentration-Time Curve From Time 0 to the Last Quantifiable Concentration (AUClast) of Eteplirsén in Plasma

End point title	Area Under Concentration-Time Curve From Time 0 to the Last Quantifiable Concentration (AUClast) of Eteplirsén in Plasma
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End point description:

The Safety Set was used for PK analysis and included all participants who were enrolled and received at least 1 dose of eteplirsén during the study. PK data were not collected for participants who received 4 mg of eteplirsén. Here, 'n' signifies number of participants evaluable at the specified timepoint.

End point type	Secondary
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End point timeframe:

Pre-infusion, immediately prior to end of infusion, and approximately 1-3 hours and 6-8 hours after completion of infusion during Weeks 2 (2 mg/kg dose level), 6 (10 mg/kg dose level), 8 (20 mg/kg dose level), and 10 and 24 (30 mg/kg dose level)

End point values	Cohort 1: Age 24 to 48 Months	Cohort 2: Age 6 to <24 Months		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	6		
Units: µg*hr/mL				
geometric mean (geometric coefficient of variation)				
2 mg/kg (Week 2 [n= 8, 5])	13.8 (± 118)	6.13 (± 73.1)		
10 mg/kg (Week 6)	56.1 (± 57.2)	27.8 (± 113)		
20 mg/kg (Week 8)	92.1 (± 94.7)	81.4 (± 89.6)		
30 mg/kg (Week 10)	119 (± 30.8)	85.0 (± 114)		
30 mg/kg (Week 24 [n=8, 6])	100 (± 42.5)	89.6 (± 43.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Amount of Drug Eliminated in Urine

End point title	Amount of Drug Eliminated in Urine
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End point description:

Amount of unchanged drug excreted in urine from time 0 to 4 hours after completion of dosing is reported. The Safety Set was used for PK analysis and included all participants who were enrolled and received at least 1 dose of eteplirsén during the study. PK data were not collected for participants who received 4 mg of eteplirsén. Here, 'Number of Subjects Analyzed' (N) signifies number of participants evaluable for this outcome measure and 'n' signifies number of participants evaluable at the specified timepoint.

End point type	Secondary
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End point timeframe:

Pre-infusion, immediately prior to end of infusion, and approximately 1-3 hours and 6-8 hours after completion of infusion during Weeks 2 (2 mg/kg dose level), 6 (10 mg/kg dose level), 8 (20 mg/kg dose level), and 10 and 24 (30 mg/kg dose level)

End point values	Cohort 1: Age 24 to 48 Months	Cohort 2: Age 6 to <24 Months		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	6		
Units: µg				
arithmetic mean (standard deviation)				
2 mg/kg dose (Week 2 [n= 3, 3])	7720 (± 9060)	1430 (± 1390)		
10 mg/kg (Week 6 [n=7, 6])	56000 (± 73300)	28700 (± 24100)		
20 mg/kg (Week 8 [n=6, 5])	102000 (± 108000)	65600 (± 47900)		
20 mg/kg (Week 8 [n=8, 6])	263000 (± 209000)	94700 (± 68500)		
30 mg/kg (Week 24 [n=7, 4])	239000 (± 140000)	147000 (± 132000)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 100

Adverse event reporting additional description:

The Safety Set included all participants who were enrolled and received at least 1 dose of eteplirsen during the study.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.1
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Reporting groups

Reporting group title	Cohort 2: Age 6 to <24 Months
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Reporting group description:

Participants between 6 to <24 months old were administered eteplirsen once every 7 days by IV infusion starting on Day 1 for up to 96 weeks. The starting dose was 2 mg/kg eteplirsen, with escalation to 4, 10, 20, and 30 mg/kg for 10 weeks and then participants continued to receive eteplirsen at 30 mg/kg for the duration of the study.

Reporting group title	Cohort 1: Age 24 to 48 Months
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Reporting group description:

Participants between 24 to 48 months old were administered eteplirsen once every 7 days by IV infusion starting on Day 1 for up to 96 weeks. The starting dose was 2 mg/kg eteplirsen, with escalation to 4, 10, 20, and 30 mg/kg for 10 weeks and then participants continued to receive eteplirsen at 30 mg/kg for the duration of the study.

Serious adverse events	Cohort 2: Age 6 to <24 Months	Cohort 1: Age 24 to 48 Months	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cohort 2: Age 6 to <24 Months	Cohort 1: Age 24 to 48 Months	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	9 / 9 (100.00%)	

Vascular disorders			
Flushing			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Haematoma			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	6 / 6 (100.00%)	7 / 9 (77.78%)	
occurrences (all)	21	21	
Catheter site swelling			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Catheter site eczema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Discomfort			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Hyperpyrexia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Infusion site extravasation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Localised oedema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	3	0	
Immune system disorders			

Allergy to chemicals subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	
Reproductive system and breast disorders Genital cyst subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Productive cough subjects affected / exposed occurrences (all)	5 / 6 (83.33%) 14 3 / 6 (50.00%) 6 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	7 / 9 (77.78%) 25 4 / 9 (44.44%) 7 2 / 9 (22.22%) 9 1 / 9 (11.11%) 1	
Psychiatric disorders Abnormal behaviour subjects affected / exposed occurrences (all) Anger subjects affected / exposed occurrences (all) Personality change subjects affected / exposed occurrences (all) Irritability subjects affected / exposed occurrences (all) Initial insomnia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1	1 / 9 (11.11%) 1 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1 1 / 9 (11.11%) 2 0 / 9 (0.00%) 0	

Investigations			
Body temperature			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	
occurrences (all)	1	3	
Blood iron decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Amylase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Body temperature increased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	
occurrences (all)	3	2	
Haemophilus test positive			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Streptococcus test positive			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 6 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
Head injury			
subjects affected / exposed	2 / 6 (33.33%)	5 / 9 (55.56%)	
occurrences (all)	3	7	
Fall			
subjects affected / exposed	2 / 6 (33.33%)	5 / 9 (55.56%)	
occurrences (all)	5	5	
Laceration			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Procedural pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Post-traumatic pain			

subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Arthropod bite			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	2	
Joint injury			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Excoriation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Lip injury			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Penis injury			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Tracheal obstruction			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Tongue injury			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Spinal fracture			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Vaccination complication			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Congenital, familial and genetic disorders			
Haemoglobinopathy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Nervous system disorders			

Lethargy subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 3	2 / 9 (22.22%) 2	
Headache subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 9 (22.22%) 2	
Psychomotor hyperactivity subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	
Blood and lymphatic system disorders Autoimmune neutropenia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	
Hypochromic anaemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	
Iron deficiency anaemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	1 / 9 (11.11%) 1	
Cerumen impaction subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 9 (11.11%) 1	
External ear inflammation subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	
Inner ear inflammation subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	
Tympanic membrane hyperaemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	
Eye disorders			

Chalazion			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	
occurrences (all)	2	3	
Eye irritation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Visual acuity reduced			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Eye pruritus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 6 (50.00%)	5 / 9 (55.56%)	
occurrences (all)	9	6	
Vomiting			
subjects affected / exposed	4 / 6 (66.67%)	8 / 9 (88.89%)	
occurrences (all)	4	15	
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Teething			
subjects affected / exposed	2 / 6 (33.33%)	1 / 9 (11.11%)	
occurrences (all)	3	1	
Constipation			
subjects affected / exposed	1 / 6 (16.67%)	2 / 9 (22.22%)	
occurrences (all)	1	8	
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
Dental caries			
subjects affected / exposed	0 / 6 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
Dental discomfort			

subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	2	
Faeces discoloured			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 6 (16.67%)	2 / 9 (22.22%)	
occurrences (all)	1	2	
Rash			
subjects affected / exposed	1 / 6 (16.67%)	2 / 9 (22.22%)	
occurrences (all)	4	2	
Rash maculo-papular			
subjects affected / exposed	3 / 6 (50.00%)	0 / 9 (0.00%)	
occurrences (all)	8	0	
Dermatitis contact			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
Dermatitis diaper			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Rash generalised			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	
occurrences (all)	3	1	
Eczema nummular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
Miliaria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	

Erythema subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	
Pruritus generalised subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	
Rash macular subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	
Rash papular subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	3 / 9 (33.33%) 8	
Arthralgia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	5 / 6 (83.33%) 19	7 / 9 (77.78%) 27	
Rhinitis subjects affected / exposed occurrences (all)	4 / 6 (66.67%) 9	4 / 9 (44.44%) 4	
Ear infection subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 3	3 / 9 (33.33%) 6	
Gastroenteritis subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 3	3 / 9 (33.33%) 6	

Bronchitis		
subjects affected / exposed	2 / 6 (33.33%)	2 / 9 (22.22%)
occurrences (all)	2	2
Influenza		
subjects affected / exposed	2 / 6 (33.33%)	1 / 9 (11.11%)
occurrences (all)	2	1
Pharyngitis		
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)
occurrences (all)	1	2
Conjunctivitis		
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)
occurrences (all)	1	1
Eye infection		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	2	0
Upper respiratory tract infection		
subjects affected / exposed	2 / 6 (33.33%)	0 / 9 (0.00%)
occurrences (all)	4	0
Gastrointestinal viral infection		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	1	0
Hand-foot-and-mouth disease		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	1	0
Hordeolum		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	1	0
Lower respiratory tract infection		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	1	0
Molluscum contagiosum		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	1
Otitis media acute		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	2	0

Roseola			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Varicella			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	2 / 6 (33.33%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
Increased appetite			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Hyposideraemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 February 2020	To reflect updates made to recently approved language from other recent Sarepta protocol amendments.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported