



## Clinical trial results:

### An Open-Label, Multi-Center Study to Evaluate the Safety, Efficacy and Tolerability of Eteplirsen in Early Stage Duchenne Muscular Dystrophy Summary

EudraCT number	2016-005023-92
Trial protocol	Outside EU/EEA
Global end of trial date	17 December 2018

#### Results information

Result version number	v1
This version publication date	22 September 2019
First version publication date	22 September 2019

#### Trial information

##### Trial identification

Sponsor protocol code	4658-203
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02420379
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Sarepta Therapeutics, Inc.
Sponsor organisation address	215 First Street, Cambridge, United States, MA, 02142
Public contact	Medical Director, Sarepta Therapeutics, Inc., +1 617274 4000, clinicaltrials@sarepta.com
Scientific contact	Medical Director, Sarepta Therapeutics, Inc., +1 617274 4000, 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?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 May 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	17 December 2018
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of eteplirsen in subjects with Duchenne muscular dystrophy (DMD) between 4 and 6 years of age who are amenable to exon 51 skipping.

Protection of trial subjects:

Written informed consent from each patient or patient's parent(s) or legal guardian(s), if applicable, and written assent from each patient, if applicable, were obtained before any study-specific screening or baseline period evaluations were performed. The anonymity of participating patients will be maintained to the extent required by applicable laws and in accordance with current HIPAA standards. This study was designed and monitored in accordance with Sponsor procedures, which complied with the ethical principles of Good Clinical Practice (GCP) as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 May 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United States: 33
Worldwide total number of subjects	33
EEA total number of subjects	0

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)	0
Children (2-11 years)	33
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 13 sites in the United States from 11 May 2015 to 17 December 2018

### Pre-assignment

Screening details:

A total of 33 subjects were enrolled in the study treatment.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	Eteplirsen 30 mg/kg
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Arm description:

Subjects with Duchenne muscular dystrophy (DMD) amenable to exon 51 skipping received eteplirsen 30 milligram per kilogram (mg/kg) intravenous (IV) infusions, once weekly, for 96 weeks.

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

Dosage and administration details:

Subjects received eteplirsen 30 mg/kg IV infusion once weekly.

<b>Arm title</b>	Control Group (Untreated)
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Arm description:

Subjects with DMD not amenable to exon 51 skipping were observed for 96 weeks.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Eteplirsen 30 mg/kg	Control Group (Untreated)
Started	26	7
Completed	25	3
Not completed	1	4
Consent withdrawn by subject	-	3
Subject was unable to complete due to schooling	-	1
Subject transitioned to commercial drug	1	-



## Baseline characteristics

### Reporting groups

Reporting group title	Eteplirsen 30 mg/kg
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Reporting group description:

Subjects with Duchenne muscular dystrophy (DMD) amenable to exon 51 skipping received eteplirsen 30 milligram per kilogram (mg/kg) intravenous (IV) infusions, once weekly, for 96 weeks.

Reporting group title	Control Group (Untreated)
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Reporting group description:

Subjects with DMD not amenable to exon 51 skipping were observed for 96 weeks.

Reporting group values	Eteplirsen 30 mg/kg	Control Group (Untreated)	Total
Number of subjects	26	7	33
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	5.0	5.0	
standard deviation	± 0.82	± 1.00	-
Gender categorical			
Units: Subjects			
Female	0	0	0
Male	26	7	33
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	1	3
Black	1	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
White	22	6	28
Other	1	0	1
Ethnicity			
Units: Subjects			
Hispanic or Latino	5	0	5
Not Hispanic or Latino	21	7	28

## End points

### End points reporting groups

Reporting group title	Eteplirsen 30 mg/kg
Reporting group description: Subjects with Duchenne muscular dystrophy (DMD) amenable to exon 51 skipping received eteplirsen 30 milligram per kilogram (mg/kg) intravenous (IV) infusions, once weekly, for 96 weeks.	
Reporting group title	Control Group (Untreated)
Reporting group description: Subjects with DMD not amenable to exon 51 skipping were observed for 96 weeks.	

### Primary: Number of Subjects with Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects with Treatment Emergent Adverse Events (TEAEs) <sup>[1]</sup>
End point description: An AE was any untoward medical occurrence in a subject that did not necessarily have a causal relationship with the study drug. A Serious adverse event (SAE) was an AE resulting in any of the following outcomes: death; Life-threatening event; Required or prolonged inpatient hospitalization; persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent adverse events were events that developed or worsened during the on-treatment period (defined as time from first dose of study drug and up to 28 days after last dose of study drug [up to 100 weeks]) that were absent before treatment or that worsened relative to pre-treatment state. AEs included both serious and non-serious adverse events. Full set includes all subjects who are enrolled in the eteplirsen group and received at least 1 dose of eteplirsen as well as all subjects who were enrolled in the untreated group and had at least 1 assessment post-enrollment assessment.	
End point type	Primary
End point timeframe: Baseline up to 100 weeks	
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: No statistical testing was performed for the primary end point.	

End point values	Eteplirsen 30 mg/kg	Control Group (Untreated)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	7		
Units: subjects	26	5		

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities Reported as TEAEs

End point title	Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities Reported as TEAEs <sup>[2]</sup>
End point description: Laboratory parameters included hematology, serum chemistry (SC), urinalysis and coagulation. Number of subjects with at least one potentially clinically significant abnormal findings were reported as TEAEs.	

The Investigator determined whether abnormal assessment results were clinically significant or not clinically significant. Clinical significance was defined as any variation in assessment results that had medical relevance resulting in an alteration in medical care. Full analysis set includes all subjects who are enrolled in the eteplirsen group and receive at least 1 dose of eteplirsen as well as all subjects who are enrolled in the untreated group who have at least 1 assessment post-enrollment assessment.

End point type	Primary
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End point timeframe:

Baseline up to 100 weeks

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: No statistical testing was performed for the primary end point.

End point values	Eteplirsen 30 mg/kg	Control Group (Untreated)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	7		
Units: Subjects				
SC: Blood creatine phosphokinase increased	1	0		
Hematology: Anaemia	1	0		
Hematology: Iron deficiency Anaemia	1	0		
Coagulation: Thrombocytopenia	0	0		
Urinalysis: chromaturia	3	0		
Urinalysis: pollakiuria	1	0		

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Subjects With Potentially Clinically Significant Abnormalities in Vital Signs Reported as TEAEs

End point title	Number of Subjects With Potentially Clinically Significant Abnormalities in Vital Signs Reported as TEAEs <sup>[3]</sup>
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End point description:

Vital sign parameters included systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), and body temperature. Number of subjects with at least one potentially clinically significant abnormal vital sign findings were reported as TEAEs. The Investigator determined whether abnormal assessment results were clinically significant or not clinically significant. Clinical significance was defined as any variation in assessment results that had medical relevance resulting in an alteration in medical care. Full analysis set includes all subjects who are enrolled in the eteplirsen group and receive at least 1 dose of eteplirsen as well as all subjects who are enrolled in the untreated group who have at least 1 assessment post-enrollment assessment.

End point type	Primary
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End point timeframe:

Baseline up to 100 weeks

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: No statistical testing was performed for the primary end point.



End point values	Eteplirsen 30 mg/kg	Control Group (Untreated)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	7		
Units: Subjects				
Pyrexia	11	1		
Pulse pressure increased	1	0		
Tachycardia	1	0		

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Subjects With at Least One Abnormal Physical Examination Finding

End point title	Number of Subjects With at Least One Abnormal Physical Examination Finding <sup>[4]</sup>
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End point description:

Physical examinations, full and brief, were performed by the Investigator, a physician Sub-Investigator, or a Nurse Practitioner (if licensed in the state or province to perform physical examinations). Full physical examinations included examination of general appearance; head, ears, eyes, nose, and throat; heart; lungs; chest; abdomen; skin; lymph nodes; and musculoskeletal and neurological systems. Number of subjects with at least one abnormal physical examination finding was reported. Full analysis set includes all subjects who are enrolled in the eteplirsen group and receive at least 1 dose of eteplirsen as well as all subjects who are enrolled in the untreated group who have at least 1 assessment post-enrollment assessment.

End point type	Primary
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End point timeframe:

Baseline up to 100 weeks

Notes:

[4] - 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: No statistical testing was performed for the primary end point.

End point values	Eteplirsen 30 mg/kg	Control Group (Untreated)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	7		
Units: Subjects	26	7		

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Subjects With Abnormalities in Electrocardiograms (ECGs) Reported as TEAEs

End point title	Number of Subjects With Abnormalities in Electrocardiograms (ECGs) Reported as TEAEs <sup>[5]</sup>
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End point description:

Twelve-lead ECGs and Holter ECGs were performed at a consistent time of day throughout the study. Cardiac function events included cardiomegaly, tachycardia, and dyspnoea, each of which were non-

serious, mild in severity, and considered unrelated to eteplirsen by the Investigator. Electrocardiograms were performed only after the patient was in the supine position, resting, and quiet for a minimum of 15 minutes. The ECG was manually reviewed and interpreted by medically qualified personnel using a central vendor according to prespecified criteria. Number of Subjects with at least one abnormalities in ECGs were reported as TEAEs. Full analysis set includes all subjects who are enrolled in the eteplirsen group and receive at least 1 dose of eteplirsen as well as all subjects who are enrolled in the untreated group who have at 1 assessment post-enrollment assessment.

End point type	Primary
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End point timeframe:

Baseline up to 96 weeks

Notes:

[5] - 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: No statistical testing was performed for the primary end point.

End point values	Eteplirsen 30 mg/kg	Control Group (Untreated)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	7		
Units: Subjects				
Tachycardia	1	0		

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Subjects With Abnormalities in Echocardiograms (ECHO) Reported as TEAEs

End point title	Number of Subjects With Abnormalities in Echocardiograms (ECHO) Reported as TEAEs <sup>[6]</sup>
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End point description:

Standard, 2-dimensional ECHOs were performed at a consistent time of day throughout the study. Cardiac function events included cardiomegaly, tachycardia, and dyspnoea, each of which were non-serious, mild in severity, and considered unrelated to eteplirsen by the Investigator. The ECHO was reviewed and interpreted by medically qualified personnel using a central vendor according to prespecified criteria. Ejection fraction was noted. Number of subjects with at least one abnormalities in ECHO were reported as TEAEs. Full analysis set includes all subjects who are enrolled in the eteplirsen group and receive at least 1 dose of eteplirsen as well as all subjects who are enrolled in the untreated group who have at least 1 assessment post-enrollment assessment.

End point type	Primary
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End point timeframe:

Baseline up to 96 weeks

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: No statistical testing was performed for the primary end point.

End point values	Eteplirsen 30 mg/kg	Control Group (Untreated)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	7		
Units: Subjects				
cardiomegaly	1	0		

## **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to 100 weeks

Adverse event reporting additional description:

Safety population included all subjects who received at least 1 dose of eteplirsen and Control group.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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### Reporting groups

Reporting group title	Eteplirsen 30 mg/kg
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Reporting group description:

Subjects received eteplirsen 30 mg/kg IV infusions, weekly, for 96 weeks.

Reporting group title	Untreated (Control Group)
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Reporting group description:

Subjects with Duchenne muscular dystrophy (DMD) not amenable to exon 51 skipping was observed for 96 weeks.

Serious adverse events	Eteplirsen 30 mg/kg	Untreated (Control Group)	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 26 (15.38%)	0 / 7 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Foreign body			
subjects affected / exposed	1 / 26 (3.85%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Coxsackie viral infection			

subjects affected / exposed	1 / 26 (3.85%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 26 (3.85%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection			
subjects affected / exposed	1 / 26 (3.85%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

<b>Non-serious adverse events</b>	Eteplirsen 30 mg/kg	Untreated (Control Group)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 26 (100.00%)	5 / 7 (71.43%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	2 / 26 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Surgical and medical procedures			
Adenoidectomy			
subjects affected / exposed	0 / 26 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Myringotomy			
subjects affected / exposed	0 / 26 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Orchidopexy			
subjects affected / exposed	0 / 26 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed occurrences (all)	11 / 26 (42.31%) 22	1 / 7 (14.29%) 1	
Catheter site pain subjects affected / exposed occurrences (all)	3 / 26 (11.54%) 3	0 / 7 (0.00%) 0	
Catheter site bruise subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	0 / 7 (0.00%) 0	
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	3 / 26 (11.54%) 7	0 / 7 (0.00%) 0	
Hypersensitivity subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	1 / 7 (14.29%) 1	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	23 / 26 (88.46%) 57	3 / 7 (42.86%) 3	
Rhinorrhoea subjects affected / exposed occurrences (all)	13 / 26 (50.00%) 18	0 / 7 (0.00%) 0	
Nasal congestion subjects affected / exposed occurrences (all)	10 / 26 (38.46%) 18	0 / 7 (0.00%) 0	
Epistaxis subjects affected / exposed occurrences (all)	5 / 26 (19.23%) 5	0 / 7 (0.00%) 0	
Oropharyngeal pain subjects affected / exposed occurrences (all)	4 / 26 (15.38%) 5	0 / 7 (0.00%) 0	
Productive cough subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 3	0 / 7 (0.00%) 0	
Upper respiratory tract congestion			

subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 3	0 / 7 (0.00%) 0	
Psychiatric disorders Aggression subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	0 / 7 (0.00%) 0	
Investigations Cardiac murmur subjects affected / exposed occurrences (all)	4 / 26 (15.38%) 5	0 / 7 (0.00%) 0	
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	9 / 26 (34.62%) 37	0 / 7 (0.00%) 0	
Contusion subjects affected / exposed occurrences (all)	5 / 26 (19.23%) 6	0 / 7 (0.00%) 0	
Procedural pain subjects affected / exposed occurrences (all)	4 / 26 (15.38%) 5	0 / 7 (0.00%) 0	
Skin abrasion subjects affected / exposed occurrences (all)	4 / 26 (15.38%) 4	0 / 7 (0.00%) 0	
Scratch subjects affected / exposed occurrences (all)	3 / 26 (11.54%) 3	0 / 7 (0.00%) 0	
Head injury subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 3	0 / 7 (0.00%) 0	
Sunburn subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	0 / 7 (0.00%) 0	
Ligament sprain subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	1 / 7 (14.29%) 1	
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	10 / 26 (38.46%) 16	0 / 7 (0.00%) 0	
Migraine subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 3	0 / 7 (0.00%) 0	
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	7 / 26 (26.92%) 9	0 / 7 (0.00%) 0	
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	11 / 26 (42.31%) 18	2 / 7 (28.57%) 3	
Diarrhoea subjects affected / exposed occurrences (all)	7 / 26 (26.92%) 10	1 / 7 (14.29%) 1	
Abdominal pain subjects affected / exposed occurrences (all)	5 / 26 (19.23%) 5	0 / 7 (0.00%) 0	
Abdominal pain upper subjects affected / exposed occurrences (all)	5 / 26 (19.23%) 12	0 / 7 (0.00%) 0	
Constipation subjects affected / exposed occurrences (all)	3 / 26 (11.54%) 4	1 / 7 (14.29%) 1	
Nausea subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	1 / 7 (14.29%) 1	
Dental caries subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	0 / 7 (0.00%) 0	
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	13 / 26 (50.00%) 20	0 / 7 (0.00%) 0	
Dermatitis contact			



subjects affected / exposed occurrences (all)	3 / 26 (11.54%) 3	0 / 7 (0.00%) 0	
Keloid scar subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	0 / 7 (0.00%) 0	
Rash pruritic subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	0 / 7 (0.00%) 0	
Renal and urinary disorders Chromaturia subjects affected / exposed occurrences (all)	3 / 26 (11.54%) 3	0 / 7 (0.00%) 0	
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all)	8 / 26 (30.77%) 18	0 / 7 (0.00%) 0	
Arthralgia subjects affected / exposed occurrences (all)	6 / 26 (23.08%) 9	0 / 7 (0.00%) 0	
Back pain subjects affected / exposed occurrences (all)	4 / 26 (15.38%) 4	0 / 7 (0.00%) 0	
Muscle spasms subjects affected / exposed occurrences (all)	4 / 26 (15.38%) 5	0 / 7 (0.00%) 0	
Muscular weakness subjects affected / exposed occurrences (all)	4 / 26 (15.38%) 4	0 / 7 (0.00%) 0	
Musculoskeletal pain subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	0 / 7 (0.00%) 0	
Scoliosis subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	1 / 7 (14.29%) 1	
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	16 / 26 (61.54%)	2 / 7 (28.57%)	
occurrences (all)	27	2	
Upper respiratory tract infection			
subjects affected / exposed	11 / 26 (42.31%)	1 / 7 (14.29%)	
occurrences (all)	20	1	
Ear infection			
subjects affected / exposed	8 / 26 (30.77%)	1 / 7 (14.29%)	
occurrences (all)	15	1	
Influenza			
subjects affected / exposed	5 / 26 (19.23%)	0 / 7 (0.00%)	
occurrences (all)	7	0	
Otitis media			
subjects affected / exposed	2 / 26 (7.69%)	1 / 7 (14.29%)	
occurrences (all)	2	2	
Pharyngitis streptococcal			
subjects affected / exposed	3 / 26 (11.54%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Rhinitis			
subjects affected / exposed	3 / 26 (11.54%)	0 / 7 (0.00%)	
occurrences (all)	10	0	
Conjunctivitis			
subjects affected / exposed	2 / 26 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Gastroenteritis viral			
subjects affected / exposed	2 / 26 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Staphylococcal infection			
subjects affected / exposed	2 / 26 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Impetigo			
subjects affected / exposed	0 / 26 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	2 / 26 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	2	0	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 January 2015	Amendment 1: Added "eteplirsen-treated" to concepts and procedures relating to treated subjects versus untreated subjects; Created new schedule of events table for untreated subjects; Revised language for vital signs time points with regard to reducing the number of collections after 1 year of treatment if no infusion reaction occurred; also added language for the untreated group; Updated AE section to explain follow-up and resolution of AE; Revised overall number of subjects for trial selection.
08 June 2017	Amendment 2: Adjusted the order of endpoints and associated objectives due to recent guidance that dystrophin quantification by Western blot was preferred over assessments using immunohistochemistry; Updated the number of subjects to allow the untreated group to enroll less than 20 subjects; Added that subjects who discontinued eteplirsen dosing at Week 96 and transitioned to commercial drug did not need to complete the end-of-trial visit assessments; Clarified that the definition of analysis populations other than the safety population were provided in the Statistical Analysis Plan.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported