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	v2 (current)
This version publication date	16 January 2021
First version publication date	22 September 2019
Version creation reason	• New data added to full data set we need to incorporate secondary outcome measures

Trial information

Trial identification

Sponsor protocol code	4658-203

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)	EMEA-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	30 June 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.

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
Arm title	Eteplirsen 30 mg/kg

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.

Arm title	Control Group (Untreated) (Non-exon 51 Amenable Subjects)

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) (Non-exon 51 Amenable Subjects)
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
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) (Non-exon 51 Amenable Subjects)
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) (Non-exon 51 Amenable Subjects)	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) (Non-exon 51 Amenable Subjects)
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), Serious TEAEs and TEAEs Leading to Discontinuation

End point title	Number of Subjects with Treatment Emergent Adverse Events (TEAEs), Serious TEAEs and TEAEs Leading to Discontinuation[1]
End point description:	
AE was any untoward medical occurrence in a subject that did not necessarily have a causal relationship with the study drug. 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 endpoint.

End point values	Eteplirsen 30 mg/kg	Control Group (Untreated) (Non-exon 51 Amenable Subjects)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	7		
Units: subjects				
Subjects with TEAEs	26	5		
Subjects with Serious TEAEs	4	0		
Subjects with TEAEs leading to discontinuation	0	0		

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[2]

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

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 endpoint.

End point values	Eteplirsen 30 mg/kg	Control Group (Untreated) (Non-exon 51 Amenable Subjects)		
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		
Urinalysis: chromaturia	3	0		
Urinalysis: pollakiuria	1	0		
Coagulation: Thrombocytopenia	0	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[3]

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

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 endpoint.

End point values	Eteplirsen 30 mg/kg	Control Group (Untreated) (Non-exon 51 Amenable Subjects)		
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[4]

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. Abnormality in physical examinations was based on Investigator's discretion. 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

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 endpoint.

End point values	Eteplirsen 30 mg/kg	Control Group (Untreated) (Non-exon 51 Amenable Subjects)		
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[5]

End point description:

Twelve-lead ECGs and Holter ECGs were performed at a consistent time of day throughout the study. Electrocardiograms were performed only after the subject 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. 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

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 endpoint.

End point values	Eteplirsen 30 mg/kg	Control Group (Untreated) (Non-exon 51 Amenable Subjects)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	7		
Units: Subjects	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[6]

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. The ECHO was reviewed and interpreted by medically qualified personnel. 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

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 endpoint.

End point values	Eteplirsen 30 mg/kg	Control Group (Untreated) (Non-exon 51 Amenable Subjects)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	7		
Units: Subjects	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dystrophin Protein Levels Quantified by Western Blot at Week 48 and 96

End point title	Change From Baseline in Dystrophin Protein Levels Quantified by Western Blot at Week 48 and 96[7]

End point description:

Change from baseline in dystrophin protein levels (in muscle biopsy samples) were determined by Western blot at Week 48 and 96 was reported. For each time point, 2 blocks of tissues were analyzed by Western blot, each with 2 replicates of gels to determine the dystrophin level as compared to a healthy individual (Percent Normal). The block average value from 2 replicate gels was computed. The overall average was calculated as the mean of the block average values. The overall average values were used for all analyses. In case only 1 gel was available for a block, then that value was used as the block average value. Muscle Biopsy Set included all subjects who received at least 1 dose of eteplirsen and who had data from both baseline (pre-treatment) and Week 48 or 96 (on-treatment) muscle biopsy samples. Here, "number of subjects analysed" signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 48 and 96

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for control group (untreated) (non-exon 51 amenable subjects).

End point values	Eteplirsen 30 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Percent Normal Dystrophin Protein Level				
arithmetic mean (standard deviation)				
Change at Week 48 (n=14)	0.102 (± 0.0896)			
Change at Week 96 (n=11)	0.321 (± 0.4863)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dystrophin Intensity Levels Determined by Immunohistochemistry (IHC) at Week 48 and 96

End point title	Change From Baseline in Dystrophin Intensity Levels Determined by Immunohistochemistry (IHC) at Week 48 and 96[8]

End point description:

Change from baseline in dystrophin intensity levels (in muscle biopsy samples) was determined by Immunohistochemistry at Week 48 and 96 was reported. Muscle Biopsy Set included all subjects who received at least 1 dose of eteplirsen and who had data from both baseline (pre-treatment) and Week 48 or 96 (on-treatment) muscle biopsy samples. Data for this outcome was not planned to be collected and analyzed for control group (untreated) (non-exon 51 amenable subjects). Here, "number of subjects analysed" signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 48 and 96

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for control group (untreated) (non-exon 51 amenable subjects).

End point values	Eteplirsen 30 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Percent dystrophin positive fibers				
arithmetic mean (standard deviation)				
Change at Week 48 (n=14)	0.004 (± 0.0096)			
Change at Week 96 (n=11)	0.015 (± 0.0175)			

Statistical analyses

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

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	Eteplirsen 30 mg/kg
Reporting group description:	
Subjects received eteplirsen 30 mg/kg IV infusions, weekly, for 96 weeks.	
Reporting group title	Control Group (Untreated) (Non-exon 51 Amenable Subjects)
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	Control Group (Untreated) (Non-exon 51 Amenable Subjects)	
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 %

Non-serious adverse events	Eteplirsen 30 mg/kg	Control Group (Untreated) (Non-exon 51 Amenable Subjects)	
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	11 / 26 (42.31%)	1 / 7 (14.29%)	
occurrences (all)	22	1	
Catheter site pain			
subjects affected / exposed	3 / 26 (11.54%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Catheter site bruise			
subjects affected / exposed	2 / 26 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	3 / 26 (11.54%)	0 / 7 (0.00%)	
occurrences (all)	7	0	
Hypersensitivity			
subjects affected / exposed	0 / 26 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	23 / 26 (88.46%)	3 / 7 (42.86%)	
occurrences (all)	57	3	
Rhinorrhoea			
subjects affected / exposed	13 / 26 (50.00%)	0 / 7 (0.00%)	
occurrences (all)	18	0	
Nasal congestion			
subjects affected / exposed	10 / 26 (38.46%)	0 / 7 (0.00%)	
occurrences (all)	18	0	
Epistaxis			
subjects affected / exposed	5 / 26 (19.23%)	0 / 7 (0.00%)	
occurrences (all)	5	0	
Oropharyngeal pain			
subjects affected / exposed	4 / 26 (15.38%)	0 / 7 (0.00%)	
occurrences (all)	5	0	
Productive cough			
subjects affected / exposed	2 / 26 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Upper respiratory tract congestion			

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

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

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

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported