Clinical trial results:
A Phase 2B Efficacy and Safety Study of PTC124 in Subjects With Nonsense-Mutation-Mediated Duchenne and Becker Muscular Dystrophy

Summary

EudraCT number	2007-005478-29
Trial protocol	FR DE SE GB BE ES IT
Global end of trial date	31 December 2009

Results information

Result version number	v1 (current)
This version publication date	11 April 2020
First version publication date	11 April 2020

Trial information

Trial identification

Sponsor protocol code	PTC124-GD-007-DMD

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00592553
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	PTC Therapeutics, Inc.
Sponsor organisation address	100 Corporate Court, South Plainfield, United States, NJ 07080
Public contact	Medical Information, PTC Therapeutics, Inc., +353 1-866-562-4620, medinfo@ptcbio.com
Scientific contact	Medical Information, PTC Therapeutics International Limited, +353 19068700, medinfo@ptcbio.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	
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	05 February 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 December 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to determine the effect of ataluren on ambulation.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki (revised version of Edinburgh, Scotland, 2000) and in conformance with the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) guidance documents.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 February 2008
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 States: 78
Country: Number of subjects enrolled	United Kingdom: 21
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Australia: 11
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Sweden: 8
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Israel: 3
Worldwide total number of subjects	174
EEA total number of subjects	72

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)	156
Adolescents (12-17 years)	17
Adults (18-64 years)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 185 participants were screened for eligibility, of which 11 participants did not meet entry criteria.

Pre-assignment

Screening details:

A total of 174 eligible participants were randomized in 1:1:1 ratio to receive either placebo, low-dose ataluren, or high-dose ataluren.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Carer, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	High-Dose Ataluren

Arm description:

Participants received ataluren suspension orally 3 times a day (TID), 20 milligrams/kilogram (mg/kg) at morning, 20 mg/kg at midday, and 40 mg/kg at evening (total daily dose 80 mg/kg) for 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Ataluren
Investigational medicinal product code	PTC124
Other name	
Pharmaceutical forms	Granules for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Ataluren was administered as per the dose and schedule specified in the respective arms.

Arm title	Low-Dose Ataluren

Arm description:

Participants received ataluren suspension orally TID, 10 mg/kg at morning, 10 mg/kg at midday, and 20 mg/kg at evening (total daily dose 40 mg/kg) for 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Ataluren
Investigational medicinal product code	PTC124
Other name	
Pharmaceutical forms	Granules for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Ataluren was administered as per the dose and schedule specified in the respective arms.

Arm title	Placebo

Arm description:

Participants received placebo matched to ataluren orally TID at morning, midday, and evening for 48 weeks.

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	PTC124
Other name	
Pharmaceutical forms	Granules for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to ataluren was administered as per the dose and schedule specified in the respective arms.

Number of subjects in period 1	High-Dose Ataluren	Low-Dose Ataluren	Placebo
Started	60	57	57
As-treated Population	60	57	57
ITT Population	60	57	57
Completed	59	57	57
Not completed	1	0	0
Protocol Noncompliance	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	High-Dose Ataluren
Reporting group description:	
Participants received ataluren suspension orally 3 times a day (TID), 20 milligrams/kilogram (mg/kg) at morning, 20 mg/kg at midday, and 40 mg/kg at evening (total daily dose 80 mg/kg) for 48 weeks.	
Reporting group title	Low-Dose Ataluren
Reporting group description:	
Participants received ataluren suspension orally TID, 10 mg/kg at morning, 10 mg/kg at midday, and 20 mg/kg at evening (total daily dose 40 mg/kg) for 48 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matched to ataluren orally TID at morning, midday, and evening for 48 weeks.	

Reporting group values	High-Dose Ataluren	Low-Dose Ataluren	Placebo
Number of subjects	60	57	57
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	8.4	8.8	8.3
standard deviation	± 2.53	± 2.91	± 2.33
Sex: Female, Male Units: Subjects			
Female	0	0	0
Male	60	57	57
6-Minute Walk Distance (6MWD)			
The 6MWD test was performed in a 30-meters-long flat corridor, where the participant was instructed to walk as far as possible, back and forth around two cones, with the permission to slow down, rest, or stop if needed. Ambulation was assessed via the 6MWD test following standardized procedures by measuring the 6MWD in meters. Participants were not permitted to use assistive devices (walker, long leg braces, or short leg braces) during the 6MWD test.			
Units: meters			
arithmetic mean	358.2	350.0	359.6
standard deviation	± 103.97	± 97.55	± 87.67

Reporting group values	Total		
Number of subjects	174		
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		

Sex: Female, Male Units: Subjects			
Female	0		
Male	174		
6-Minute Walk Distance (6MWD)			
The 6MWD test was performed in a 30-meters-long flat corridor, where the participant was instructed to walk as far as possible, back and forth around two cones, with the permission to slow down, rest, or stop if needed. Ambulation was assessed via the 6MWD test following standardized procedures by measuring the 6MWD in meters. Participants were not permitted to use assistive devices (walker, long leg braces, or short leg braces) during the 6MWD test.			
Units: meters arithmetic mean standard deviation	- 		

End points

End points reporting groups

Reporting group title	High-Dose Ataluren
Reporting group description:	
Participants received ataluren suspension orally 3 times a day (TID), 20 milligrams/kilogram (mg/kg) at morning, 20 mg/kg at midday, and 40 mg/kg at evening (total daily dose 80 mg/kg) for 48 weeks.	
Reporting group title	Low-Dose Ataluren
Reporting group description:	
Participants received ataluren suspension orally TID, 10 mg/kg at morning, 10 mg/kg at midday, and 20 mg/kg at evening (total daily dose 40 mg/kg) for 48 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matched to ataluren orally TID at morning, midday, and evening for 48 weeks.	

Primary: Change From Baseline in 6MWD at Week 48

End point title	Change From Baseline in 6MWD at Week 48
End point description:	
The 6MWD test was performed in a 30-meters-long flat corridor, where the participant was instructed to walk as far as possible, back and forth around two cones, with the permission to slow down, rest, or stop if needed. Ambulation was assessed via the 6MWD test following standardized procedures by measuring the 6MWD in meters. Participants were not permitted to use assistive devices (walker, long leg braces, or short leg braces) during the 6MWD test. Intent-to-treat (ITT) population included all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. Here, 'Overall number of participants analysed' signifies participants evaluable for this endpoint.	
End point type	Primary
End point timeframe:	
Baseline, Week 48	

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	55	55	
Units: meters				
arithmetic mean (standard deviation)	-41.81 (± 89.234)	-12.86 (± 72.007)	-42.56 (± 90.046)	

Statistical analyses

Statistical analysis title	High-Dose Ataluren versus Placebo
Statistical analysis description:	
Analysis was performed using mixed model for repeated measures (MMRM) method including rank transformed 6MWD as the dependent variable; and rank transformed baseline 6MWD, treatment, visit, age (less than [<] 9 years versus [vs.] greater than or equal to [>=] 9 years) and corticosteroid use (yes vs. no) stratification factors, and interaction between treatment and visit as independent variables.	
Comparison groups	High-Dose Ataluren v Placebo

Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4756
Method	Mixed models analysis
Parameter estimate	Least Square (LS) Mean Difference
Point estimate	-30.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-114.8
upper limit	53.75
Variability estimate	Standard error of the mean
Dispersion value	42.68

Statistical analysis title	Low-Dose Ataluren versus Placebo

Statistical analysis description:

Analysis was performed using MMRM method including rank transformed 6MWD as the dependent variable; and rank transformed baseline 6MWD, treatment, visit, age (< 9 years vs. >= 9 years) and corticosteroid use (yes vs. no) stratification factors, and interaction between treatment and visit as independent variables.

Comparison groups	Low-Dose Ataluren v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.149
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	62.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.66
upper limit	147.96
Variability estimate	Standard error of the mean
Dispersion value	43.21

Secondary: Change From Baseline in Time to Stand From Supine Position at Week 48

End point title	Change From Baseline in Time to Stand From Supine Position at Week 48

End point description:

If the time taken to perform this test exceeded 30 seconds or if a participant could not perform this test due to disease progression, a value of 30 seconds was used. Change from baseline data has been reported. ITT population: all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. 'n'= participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: seconds				
arithmetic mean (standard deviation)				
Baseline (n=60, 57, 57)	12.25 (± 11.191)	10.80 (± 9.924)	11.50 (± 11.440)	
Change at Week 48 (n=59, 57, 56)	3.00 (± 5.686)	3.23 (± 5.761)	3.24 (± 7.253)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Time to Walk/Run 10 Meters at Week 48

End point title	Change From Baseline in Time to Walk/Run 10 Meters at Week 48

End point description:

If the time taken to perform this test exceeded 30 seconds or if a participant could not perform this test due to disease progression, a value of 30 seconds was used. Change from baseline data has been reported. ITT population included all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. Here, 'n' signifies participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: seconds				
arithmetic mean (standard deviation)				
Baseline (n=60, 57, 57)	7.80 (± 5.243)	7.45 (± 4.373)	6.86 (± 2.813)	
Change at Week 48 (n=59, 57, 56)	2.37 (± 6.149)	1.68 (± 5.617)	3.03 (± 6.691)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Time to Climb 4 Stairs at Week 48

End point title	Change From Baseline in Time to Climb 4 Stairs at Week 48

End point description:

If the time taken to perform this test exceeded 30 seconds or if a participant could not perform this test due to disease progression, a value of 30 seconds was used. Change from baseline data has been reported. ITT population included all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. Here, 'n' signifies participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: seconds				
arithmetic mean (standard deviation)				
Baseline (n=60, 57, 57)	7.63 (± 7.522)	6.94 (± 6.474)	6.04 (± 5.661)	
Change at Week 48 (n=59, 57, 56)	3.51 (± 6.794)	2.39 (± 4.618)	4.79 (± 7.949)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Time to Descend 4 Stairs at Week 48

End point title	Change From Baseline in Time to Descend 4 Stairs at Week 48

End point description:

If the time taken to perform this test exceeded 30 seconds or if a participant could not perform this test due to disease progression, a value of 30 seconds was used. Change from baseline data has been reported. ITT population included all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. Here, 'n' signifies participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: seconds				
arithmetic mean (standard deviation)				
Baseline (n= 60, 57, 57)	6.75 (± 7.219)	6.08 (± 5.985)	5.52 (± 5.753)	
Change at Week 48 (n=59, 57, 56)	2.95 (± 7.323)	2.41 (± 6.162)	4.03 (± 7.828)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Force Exerted During Knee Flexion and Extension, Elbow Flexion and Extension, and Shoulder Abduction at Week 48, as Assessed by Myometry

End point title	Change From Baseline in Force Exerted During Knee Flexion and Extension, Elbow Flexion and Extension, and Shoulder Abduction at Week 48, as Assessed by Myometry

End point description:

Upper and lower extremity myometry was performed using a myometer following standardized procedures. Muscle groups evaluated included knee flexors, knee extensors, elbow flexors, elbow extensors, and shoulder abductors. Bilateral assessments were done and 3 measurements were recorded from each muscle group on each side if possible. Mean values for the left and right sides were calculated. ITT population included all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. Here, 'n' signifies participants evaluable for specified categories.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: pounds				
arithmetic mean (standard deviation)				
Baseline: Knee flexion (n=60,57,57)	12.45 (± 4.684)	12.08 (± 4.217)	11.06 (± 3.494)	
Change at Week 48: Knee flexion (n=59,57,55)	0.39 (± 3.148)	-0.07 (± 3.511)	0.38 (± 2.991)	
Baseline: Knee extension (n=60,57,56)	12.71 (± 7.910)	12.81 (± 5.753)	12.96 (± 6.162)	
Change at Week 48: Knee extension (n=59,57,55)	-0.59 (± 3.511)	-0.63 (± 3.616)	-1.85 (± 3.899)	
Baseline: Elbow flexion (n=60,57,57)	8.72 (± 4.709)	7.66 (± 3.154)	8.14 (± 2.972)	
Change at Week 48: Elbow flexion (n=59,57,56)	-0.50 (± 1.832)	-0.10 (± 1.680)	-0.35 (± 1.807)	
Baseline: Elbow extension (n=60,57,57)	6.81 (± 3.815)	6.19 (± 3.083)	6.77 (± 2.785)	
Change at Week 48: Elbow extension (n=59,57,56)	-0.28 (± 1.473)	0.10 (± 1.493)	-0.51 (± 2.333)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Mean Activity Period/Day/Visit at Week 48, as Assessed by Step Activity Monitoring (SAM)

End point title	Change From Baseline in Mean Activity Period/Day/Visit at Week 48, as Assessed by Step Activity Monitoring (SAM)

End point description:

Participants were instructed to continue to wear SAM (a pedometer) for at least 9 consecutive days. SAM was used to record number of strides/minute following each visit. A stride is the leg motion that begins when foot with SAM leaves the floor and ends when same foot touches the floor again (a stride generally equals 2 steps). Mean obtained during Screening (Week -6 to -1) and following Week 1 visit were used as baseline data. For each day, an active period was defined as the first time after 3:00 AM that greater than (>) 2 strides/minute were recorded to the last time prior to midnight that >2 strides/minute were recorded. Days were deleted on which such an active period was less than (<) 50% of mean active period across all days for that participant's visit. ITT population included all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. Here, 'n'=participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: minutes				
arithmetic mean (standard deviation)				
Baseline (n= 59, 53, 54)	756.84 (± 84.612)	761.86 (± 76.984)	751.71 (± 60.513)	
Change at Week 48 (n= 56, 53, 49)	0.87 (± 57.833)	-22.23 (± 84.759)	-19.91 (± 91.960)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Mean Total Step Count/Day/Visit During the Active Periods at Week 48, as Assessed by SAM

End point title	Change From Baseline in Mean Total Step Count/Day/Visit During the Active Periods at Week 48, as Assessed by SAM

End point description:

Participants were instructed to continue to wear SAM (a pedometer) for at least 9 consecutive days. SAM was used to record the number of strides/minute following each visit. A stride is the leg motion that begins when foot with SAM leaves the floor and ends when the same foot touches the floor again (a stride generally equals 2 steps). Mean obtained during Screening (Week -6 to -1) and following Week 1 visit were used as baseline data. For each day, an active period was defined as the first time after 3:00 AM that >2 strides/minute were recorded to the last time prior to midnight that >2 strides/minute were recorded. Days were deleted on which such an active period was <50% of mean active period across all days for that participant's visit. ITT population included all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. Here, 'n'= participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: steps/day				
arithmetic mean (standard deviation)				
Baseline (n=59, 53, 54)	5302.31 (± 1907.058)	4870.13 (± 2165.522)	5602.31 (± 2023.543)	
Change at Week 48 (n=56, 53, 49)	-615.14 (± 1468.452)	-676.46 (± 1717.535)	-908.34 (± 1999.969)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Mean Total Step Count/Hour During the Active Period at Week 48, as Assessed by SAM

End point title	Change From Baseline in Mean Total Step Count/Hour During the Active Period at Week 48, as Assessed by SAM

End point description:

Participants were instructed to continue to wear SAM (a pedometer) for at least 9 consecutive days. SAM was used to record number of strides/minute following each visit. A stride is the leg motion that begins when the foot with SAM leaves the floor and ends when the same foot touches the floor again (a stride generally equals 2 steps). Mean obtained during Screening (Week -6 to -1) and following Week 1 visit were used as baseline data. For each day, an active period was defined as the first time after 3:00 AM that >2 strides/minute were recorded to the last time prior to midnight that >2 strides/minute were recorded. Days were deleted on which such an active period was <50% of the mean active period across all days for that participant's visit. ITT population included all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. Here, 'n'=participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: steps/hour				
arithmetic mean (standard deviation)				
Baseline (n=59, 53, 54)	423.67 (± 168.754)	383.62 (± 161.911)	446.37 (± 160.666)	
Change at Week 48 (n=56, 53, 49)	-44.51 (± 125.154)	-42.23 (± 126.429)	-59.62 (± 153.054)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Maximum Continuous 10-minute, 20-minute, 30-minute, and 60-minute Total Step Count at Week 48, as Assessed by SAM

End point title	Change From Baseline in Maximum Continuous 10-minute, 20-minute, 30-minute, and 60-minute Total Step Count at Week 48, as Assessed by SAM

End point description:

Participants were instructed to continue to wear SAM (a pedometer) for at least 9 consecutive days. SAM was used to record the number of strides/minute following each visit. A stride is the leg motion that begins when the foot with SAM leaves the floor and ends when the same foot touches the floor again (a stride generally equals 2 steps). Mean obtained during Screening (Week -6 to -1) and following Week 1 visit were used as baseline data. For each day, an active period was defined as the first time after 3:00 AM that >2 strides/minute were recorded to the last time prior to midnight that >2 strides/minute were recorded. Days were deleted on which such an active period was <50% of the mean active period across all days for that participant's visit. ITT population included all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. Here, 'n'=participants evaluable for specified categories.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: steps				
arithmetic mean (standard deviation)				
Baseline: 10-min step count (n=59,55,54)	35.77 (± 10.222)	32.24 (± 11.374)	36.76 (± 8.935)	
Change at Week 48: 10-min step count (n=56,54,49)	-2.77 (± 8.569)	-2.79 (± 6.355)	-3.97 (± 9.720)	
Baseline: 20-min step count (n=59,55,54)	29.13 (± 9.272)	25.68 (± 10.038)	29.74 (± 8.205)	
Change at Week 48: 20-min step count (n=56,54,49)	-2.49 (± 7.407)	-2.40 (± 5.806)	-3.55 (± 8.677)	
Baseline: 30-min step count (n=59,55,54)	25.00 (± 8.053)	22.08 (± 9.206)	25.70 (± 7.350)	
Change at Week 48: 30-min step count (n=56,54,49)	-2.08 (± 6.519)	-2.31 (± 5.505)	-3.03 (± 7.604)	
Baseline: 60-min step count (n=59,55,54)	18.58 (± 6.210)	16.52 (± 7.199)	19.50 (± 5.887)	
Change at Week 48: 60-min step count (n=56,54,49)	-1.50 (± 5.177)	-1.85 (± 4.616)	-2.33 (± 6.241)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Percentage of Time During the Active Period Spent at Low Activity (Less Than or Equal to [≤] 15 steps/minute), Medium Activity (16-30 steps/minute), and High Activity (Greater Than [>]30 Steps/minute) at Week 48

End point title	Change From Baseline in Percentage of Time During the Active Period Spent at Low Activity (Less Than or Equal to [≤] 15

	steps/minute), Medium Activity (16-30 steps/minute), and High Activity (Greater Than [>]30 Steps/minute) at Week 48

End point description:

Participants were instructed to continue to wear SAM (a pedometer) for at least 9 consecutive days. SAM was used to record number of strides/minute following each visit. A stride is the leg motion that begins when foot with SAM leaves the floor and ends when same foot touches the floor again (a stride generally equals 2 steps). Mean obtained during Screening (Week -6 to -1) and following Week 1 visit were used as baseline data. For each day, an active period was defined as the first time after 3:00 AM that greater than (>) 2 strides/minute were recorded to the last time prior to midnight that >2 strides/minute were recorded. Days were deleted on which such an active period was less than (<) 50% of mean active period across all days for that participant's visit. ITT population included all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. Here, 'n'=participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: percentage of time				
arithmetic mean (standard deviation)				
Baseline: Low activity (n=59,53,54)	32.91 (± 7.842)	32.38 (± 8.213)	32.86 (± 6.239)	
Change at Week 48: Low activity (n=56,53,49)	-2.06 (± 7.903)	-1.12 (± 8.220)	-1.11 (± 5.586)	
Baseline: Medium activity (n=59,53,54)	11.11 (± 4.013)	10.00 (± 3.656)	11.84 (± 4.304)	
Change at Week 48: Medium activity (n=56,53,49)	-1.35 (± 3.348)	-0.69 (± 3.828)	-1.92 (± 4.178)	
Baseline: High activity (n=59,53,54)	6.59 (± 4.077)	5.78 (± 3.785)	7.17 (± 3.700)	
Change at Week 48: High activity (n=54,52,48)	-0.66 (± 2.790)	-0.96 (± 2.828)	-1.03 (± 3.783)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Participant- Reported Health-Related Quality of Life (HRQL) as measured by the Pediatric Quality of Life Inventory (PedsQL) Physical, Emotional, Social, and School Functioning Domain Scores at Week 48

End point title	Change From Baseline in Participant- Reported Health-Related Quality of Life (HRQL) as measured by the Pediatric Quality of Life Inventory (PedsQL) Physical, Emotional, Social, and School Functioning Domain Scores at Week 48

End point description:

PedsQL includes generic core module (including physical, emotional, social and school functioning scales) comprises 23 questions and fatigue-specific module (including general fatigue, sleep/rest fatigue, and cognitive fatigue scales) comprises an additional 18 questions. Examples of items in each of generic core module scales include: "It is hard for me to run"; "I feel sad or blue"; "I cannot do things that other kids my age can do;" and "It is hard to pay attention in class." Each of the generic core module items was scored on a 5-point Likert response scale from 0 (never a problem) to 4 (almost always a problem). Scores were transformed on a scale from 0 to 100 (0=100, 1=75, 2=50, 3=25,

4=0), with higher scores indicating better health-related quality of life. ITT population: all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. Here, 'n'=participants evaluable for specified categories.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline: Physical function score (n=58,56,56)	63.63 (± 20.029)	59.27 (± 22.782)	61.87 (± 19.411)	
Change at Week 48: Physical function (n=54,55,50)	-0.94 (± 19.125)	2.37 (± 25.105)	-1.00 (± 24.022)	
Baseline: Emotional function score (n=58,55,56)	73.92 (± 20.418)	73.70 (± 20.223)	70.13 (± 19.332)	
Change at Week 48: Emotional function (n=54,54,50)	2.36 (± 16.742)	-1.83 (± 23.725)	4.30 (± 22.315)	
Baseline: Social function score (n=58,55,55)	67.50 (± 21.749)	65.09 (± 18.421)	63.36 (± 20.476)	
Change at Week 48: Social function (n=54,54,51)	5.37 (± 20.463)	3.89 (± 21.841)	7.75 (± 18.870)	
Baseline: School function score (n=58,55,54)	67.72 (± 19.276)	64.55 (± 20.396)	64.65 (± 17.841)	
Change at Week 48: School function (n=52,54,49)	3.61 (± 13.008)	6.11 (± 23.765)	4.06 (± 23.244)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Parent/Caregiver- Reported HRQL as measured by the PedsQL Physical, Emotional, Social, and School Functioning Domain Scores at Week 48

End point title	Change From Baseline in Parent/Caregiver- Reported HRQL as measured by the PedsQL Physical, Emotional, Social, and School Functioning Domain Scores at Week 48

End point description:

PedsQL includes generic core module (including physical, emotional, social and school functioning scales) comprises 23 questions and fatigue-specific module (including general fatigue, sleep/rest fatigue, and cognitive fatigue scales) comprises an additional 18 questions. Examples of items in each of generic core module scales include: "It is hard for me to run"; "I feel sad or blue"; "I cannot do things that other kids my age can do;" and "It is hard to pay attention in class." Each of the generic core module items was scored on a 5-point Likert response scale from 0 (never a problem) to 4 (almost always a problem). Scores were transformed on a scale from 0 to 100 (0=100, 1=75, 2=50, 3=25, 4=0), with higher scores indicating better health-related quality of life. ITT population: all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. Here, 'n'=participants evaluable for specified categories.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline: Physical function score (n=60,56,57)	56.15 (± 19.955)	54.96 (± 20.592)	51.47 (± 19.274)	
Change at Week 48: Physical function (n=59,56,57)	0.03 (± 17.088)	-3.10 (± 16.550)	0.23 (± 23.712)	
Baseline: Emotional function score (n=60,56,57)	70.08 (± 16.836)	69.11 (± 18.711)	65.96 (± 17.964)	
Change at Week 48: Emotional function (n=59,56,57)	4.07 (± 15.382)	3.39 (± 18.068)	1.21 (± 17.794)	
Baseline: Social function score (n=60,56,57)	61.58 (± 15.825)	62.77 (± 16.540)	55.79 (± 18.269)	
Change at Week 48: Social function (n=59,56,57)	-0.40 (± 18.470)	-1.09 (± 14.268)	3.71 (± 14.130)	
Baseline: School function score (n=60,56,57)	66.17 (± 18.258)	66.16 (± 16.320)	61.93 (± 13.587)	
Change at Week 48: School function (n=58,56,56)	2.73 (± 18.490)	-2.32 (± 15.462)	3.48 (± 13.913)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Participant-Reported HRQL as measured by the Total Fatigue Scale Score at Week 48

End point title	Change From Baseline in Participant-Reported HRQL as measured by the Total Fatigue Scale Score at Week 48

End point description:

The fatigue-specific module (including general fatigue, sleep/rest fatigue, and cognitive fatigue scales) comprises an additional 18 questions. Fatigue-specific module obtains information relating to items such as: "I feel too tired to do things that I like to do"; "I spend a lot of time in bed"; and "I have trouble remembering more than one thing at a time;" Each of the fatigue-specific module items was scored on a 5-point Likert response scale from 0 (never a problem) to 4 (almost always a problem). Scores were transformed on a scale from 0 to 100 (0=100, 1=75, 2=50, 3=25, 4=0), with higher scores indicating less fatigue. Total score was the sum of all items over the number of items answered on all scales. ITT population included all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. Here, 'n'=participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 58, 55, 54)	69.47 (± 16.525)	71.62 (± 16.474)	69.70 (± 15.263)	
Change at Week 48 (n= 55, 54, 52)	6.95 (± 13.460)	0.45 (± 23.068)	3.92 (± 16.512)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Parent/Caregiver-Reported HRQL as measured by the Total Fatigue Scale Score at Week 48

End point title	Change From Baseline in Parent/Caregiver-Reported HRQL as measured by the Total Fatigue Scale Score at Week 48

End point description:

The fatigue-specific module (including general fatigue, sleep/rest fatigue, and cognitive fatigue scales) comprises an additional 18 questions. Fatigue-specific module obtains information relating to items such as: "I feel too tired to do things that I like to do"; "I spend a lot of time in bed"; and "I have trouble remembering more than one thing at a time;" Each of the fatigue-specific module items was scored on a 5-point Likert response scale from 0 (never a problem) to 4 (almost always a problem). Scores were transformed on a scale from 0 to 100 (0=100, 1=75, 2=50, 3=25, 4=0), with higher scores indicating less fatigue. Total score was the sum of all items over the number of items answered on all scales. ITT population included all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. Here, 'n'=participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=60, 56, 57)	73.39 (± 13.671)	70.71 (± 12.720)	68.27 (± 13.170)	
Change at Week 48 (n=58,54, 57)	1.97 (± 13.873)	1.27 (± 12.095)	2.51 (± 12.039)	

Statistical analyses

No statistical analyses for this end point

Secondary: Parent/Caregiver-Reported Treatment Satisfaction Questionnaire for Medication (TSQM) Score

End point title	Parent/Caregiver-Reported Treatment Satisfaction Questionnaire for Medication (TSQM) Score

End point description:

TSQM consisted of 14 questions(Q) in 4 domains: Effectiveness (Q 1-3 scored as 1 [extremely dissatisfied] to 7 [extremely satisfied]), Side Effects (Q 4 scored:0 [no] or 1 [yes]; Q 5 scored:1 [extreme bothersome] to 5 [not at all bothersome]; Q 6 - 8 scored:1 [great deal] to 5 [not at all]), Convenience (Q 9 and 10 scored:1 [extreme difficult] to 7[extreme easy]; Q 11 scored:1 [extremely inconvenient] to 5 [extremely convenient]) and Global Satisfaction (Q 12 scored:1 [not at all confident] to 7 [extreme confident]; Q 13 scored:1 [not at all certain] to 5[extremely certain]; Q 14 scored:1 [extremely dissatisfied] to 5 [extremely satisfied]). Scores of each of the domains were added together and an algorithm was used to create a score of 0-100, with higher scores=better treatment satisfaction. ITT population:participants who were randomized & received any study drug; had a valid baseline, & at least 1 valid post-baseline 6MWD value. 'n'=participants evaluable for specified categories.

End point type	Secondary

End point timeframe:

Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: units on a scale				
arithmetic mean (standard deviation)				
Effectiveness score (n=53,55,53)	55.97 (± 27.796)	54.60 (± 22.307)	51.26 (± 23.536)	
Side-effects score (n=55,56,55)	96.36 (± 11.199)	97.77 (± 7.578)	96.89 (± 8.874)	
Convenience score (n=57,56,55)	55.85 (± 17.008)	58.23 (± 19.040)	60.91 (± 16.665)	
Global satisfaction score (n=55,56,55)	61.04 (± 25.967)	61.19 (± 23.691)	57.56 (± 21.851)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Participant/Caregiver-Reported Number of Daily Accidental Falls at Week 48

End point title	Change From Baseline in Participant/Caregiver-Reported Number of Daily Accidental Falls at Week 48

End point description:

Number of falls was determined by daily diary records maintained by participants and/or parent/caregivers. ITT population included all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. Here, 'n' signifies participants evaluable for this endpoint at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: falls/day				
arithmetic mean (standard deviation)				
Baseline (n=54, 48, 48)	0.40 (± 0.597)	0.27 (± 0.480)	0.54 (± 0.943)	
Change at Week 48 (n=52, 47, 44)	-0.10 (± 0.466)	-0.06 (± 0.501)	0.20 (± 1.282)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Number of Digits Recalled Forwards and Backwards on Digit Span Task at Week 48

End point title	Change From Baseline in Number of Digits Recalled Forwards and Backwards on Digit Span Task at Week 48

End point description:

Basic attention and working memory was measured using the digit span task. A series of digits (0-9) were presented to the child in an auditory format only. The task had 2 parts; in the forward condition, the child was requested to repeat back the digits in the order they were presented and in the backward condition, he was requested to reverse the order of presentation. A raw score of the total number of correct responses was converted to an age-scaled-score (z-score) by subtracting the corresponding mean and dividing by the corresponding standard deviation of a reference population for that age. ITT population included all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. Here, 'n'=participants evaluable for this endpoint for specified categories.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: z-score				
arithmetic mean (standard deviation)				
Baseline: Forward condition (n=59,56,55)	3.59 (± 2.554)	2.89 (± 2.180)	2.84 (± 1.675)	
Change at Week 48: Forward condition (n=57,54,52)	0.39 (± 1.677)	0.50 (± 1.767)	0.40 (± 1.550)	
Baseline: Backward condition (n=59,56,54)	1.73 (± 1.846)	1.70 (± 1.868)	1.59 (± 1.460)	
Change at Week 48: Backward condition (57,54,51)	0.56 (± 1.500)	0.33 (± 1.441)	0.59 (± 1.203)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Heart Rate Before, During, and After Each 6MWT at Week 48, as Assessed by Heart Rate Monitoring With the Polar® RS400

End point title	Change From Baseline in Heart Rate Before, During, and After Each 6MWT at Week 48, as Assessed by Heart Rate Monitoring With the Polar® RS400

End point description:

Heart rate was measured with a Polar RS400 heart rate monitor, which consists of a transmitter strap worn around the chest and a wristwatch receiver. Monitor produces a digital text file with 1 value per minute that represents mean heart rate for that minute. Mean heart rates values were collected prior to, during, and after the 6MWD. The participant rested for 5 minutes in a sitting position prior to the 6MWD, and the mean heart rate for the last minute of this rest period was collected and documented as the resting heart rate. During the 6MWT, the mean heart rate was collected and documented as the active heart rate. After completing the 6MWT and resting for 3 minutes, the mean heart rate for 1 minute was collected and documented as the recovery heart rate. ITT population included all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. Here, 'n'=participants evaluable for specified categories.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: beats/minute				
arithmetic mean (standard deviation)				
Baseline: Resting heart rate (n=60,57,57)	105.47 (± 12.908)	109.70 (± 9.908)	104.07 (± 11.588)	
Change at Week 48: Resting heart rate (n=54,53,50)	-0.63 (± 13.008)	-0.36 (± 10.223)	-0.26 (± 15.614)	
Baseline: Active heart rate (n=60,56,57)	142.67 (± 18.070)	141.77 (± 15.574)	136.67 (± 20.713)	
Change at Week 48: Active heart rate (n=53,49,48)	-5.00 (± 21.976)	2.39 (± 19.095)	1.65 (± 21.295)	
Baseline: Recovery heart rate (n=60,56,57)	109.90 (± 12.633)	113.48 (± 10.340)	107.86 (± 12.066)	
Change at Week 48:Recovery heart rate (n=53,49,48)	-0.23 (± 13.475)	-1.33 (± 13.270)	0.54 (± 15.181)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Serum Concentration of Creatine Kinase (CK) at Week 48

End point title	Change From Baseline in Serum Concentration of Creatine Kinase (CK) at Week 48

End point description:

Blood samples collected for chemistry assays were used to quantify serum CK concentrations. Serum CK was assessed as a potential biomarker for muscle fragility, with a reduction in serum CK considered to be a positive outcome. ITT population included all participants who were randomized and received any study treatment; and had a valid baseline, and at least one valid post-baseline 6MWD value. Here, 'n' signifies participants evaluable for this endpoint at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: units/liter (U/L)				
arithmetic mean (standard deviation)				
Baseline (n= 60, 57, 57)	10853.65 (± 6251.136)	12084.70 (± 7772.631)	10569.60 (± 6488.477)	
Change at Week 48 (n= 58, 57, 55)	-1680.09 (± 4264.769)	-2146.32 (± 7151.944)	-1235.13 (± 4323.943)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Pre-Treatment Visit (1 Week Prior to Baseline Visit) in Biceps Muscle Dystrophin Expression at Post-Treatment Visit (Week 36), as Determined by Immunofluorescence

End point title	Percent Change From Pre-Treatment Visit (1 Week Prior to Baseline Visit) in Biceps Muscle Dystrophin Expression at Post-Treatment Visit (Week 36), as Determined by Immunofluorescence

End point description:

Immunofluorescence evidence of a change in dystrophin expression on biceps muscle biopsy was defined as an increase in the staining of the sarcolemmal membrane with an antibody to the C-terminal portion of the dystrophin protein (excluding revertant fibers) between the pre-treatment (1 week prior to Baseline visit) and post-treatment (Week 36) biopsies. The biceps muscle was biopsied from one arm for confirmation of the absence or reduced levels of dystrophin prior to treatment initiation and from the other arm to assess for production of dystrophin post-treatment. As-treated population included all randomized participants who actually received any study treatment. Here, `n' signifies participants evaluable for this endpoint at specified timepoint.

End point type	Secondary

End point timeframe:

Pre-Treatment (1 week prior to baseline), post-treatment (Week 36)

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: percent change				
arithmetic mean (standard deviation)				
Pre-treatment (n=60,55,56)	336.096 (± 138.9753)	359.797 (± 142.7361)	357.271 (± 139.6650)	
Percent change post-treatment (n=59,55,56)	-1.278 (± 27.7432)	-2.128 (± 28.8287)	-0.898 (± 19.2112)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants With Treatment-Emergent Adverse Events (AEs)

End point title	Percentage of Participants With Treatment-Emergent Adverse Events (AEs)

End point description:

An AE was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. Serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. AEs included both SAEs and non-serious AEs. Treatment-emergent adverse event (TEAE) was defined as an adverse event that occurred or worsened in the period extending from first dose of study drug to 6 weeks after the last dose of study drug. A summary of other non-serious AEs and all SAEs, regardless of causality is located in the 'Reported AE section'. As-treated population included all randomized participants who actually received any study treatment.

End point type	Other pre-specified

End point timeframe:

Baseline up to Week 54

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: percentage of participants				
number (not applicable)	95.0	96.5	98.2	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Study Drug Compliance

End point title	Study Drug Compliance

End point description:

Study drug compliance was assessed by participant daily diary and quantification of used and unused study drug. Compliance was assessed in terms of the percentage of drug actually taken relative to the amount that should have been taken during the study. As-treated population included all randomized participants who actually received any study treatment.

End point type	Other pre-specified

End point timeframe:

Baseline to Week 48

End point values	High-Dose Ataluren	Low-Dose Ataluren	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	57	57	
Units: percentage of drug				
median (full range (min-max))	97.87 (34.9 to 99.6)	97.03 (64.5 to 99.8)	97.74 (76.6 to 99.9)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to 6 weeks after the last dose of study drug (Week 54)	
Adverse event reporting additional description:	
As-treated population included all randomized participants who actually received any study treatment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	9.1

Reporting groups	
Reporting group title	High-Dose Ataluren
Reporting group description:	
Participants received ataluren suspension orally TID, 20 mg/kg at morning, 20 mg/kg at midday, and 40 mg/kg at evening (total daily dose 80 mg/kg) for 48 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matched to ataluren orally TID at morning, midday, and evening for 48 weeks.	
Reporting group title	Low-Dose Ataluren
Reporting group description:	
Participants received ataluren suspension orally TID, 10 mg/kg at morning, 10 mg/kg at midday, and 20 mg/kg at evening (total daily dose 40 mg/kg) for 48 weeks.	

Serious adverse events	High-Dose Ataluren	Placebo	Low-Dose Ataluren
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 60 (3.33%)	3 / 57 (5.26%)	2 / 57 (3.51%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Supraventricular tachycardia			

subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Grand mal convulsion			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	High-Dose Ataluren	Placebo	Low-Dose Ataluren
Total subjects affected by non-serious adverse events			
subjects affected / exposed	58 / 60 (96.67%)	57 / 57 (100.00%)	56 / 57 (98.25%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Skin papilloma			
subjects affected / exposed	1 / 60 (1.67%)	1 / 57 (1.75%)	2 / 57 (3.51%)
occurrences (all)	1	1	3
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 60 (1.67%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	1	1	0
Hypertension			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	4 / 57 (7.02%)
occurrences (all)	0	1	6
Hypotension			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Pallor			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			
Endodontic procedure			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Tooth extraction			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Adhesion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Asthenia			

subjects affected / exposed	4 / 60 (6.67%)	2 / 57 (3.51%)	3 / 57 (5.26%)
occurrences (all)	5	2	4
Disease progression			
subjects affected / exposed	5 / 60 (8.33%)	6 / 57 (10.53%)	4 / 57 (7.02%)
occurrences (all)	5	6	4
Energy increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	6 / 60 (10.00%)	2 / 57 (3.51%)	2 / 57 (3.51%)
occurrences (all)	6	3	2
Feeling abnormal			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Feeling hot			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Gait disturbance			
subjects affected / exposed	4 / 60 (6.67%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	4	1	0
Ill-defined disorder			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	4	0	0
Malaise			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	2 / 57 (3.51%)
occurrences (all)	0	1	2
Pain			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	8 / 60 (13.33%)	12 / 57 (21.05%)	14 / 57 (24.56%)
occurrences (all)	10	14	21
Thirst			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			

Drug hypersensitivity			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Hypersensitivity			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	2	0	0
Seasonal allergy			
subjects affected / exposed	0 / 60 (0.00%)	4 / 57 (7.02%)	1 / 57 (1.75%)
occurrences (all)	0	4	1
Reproductive system and breast disorders			
Balanitis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	1	1	0
Genital erythema			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Pruritus genital			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	1	0	1
Testicular pain			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Bronchial hyperreactivity			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	15 / 60 (25.00%)	13 / 57 (22.81%)	9 / 57 (15.79%)
occurrences (all)	27	19	14
Dyspnoea			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Epistaxis			

subjects affected / exposed	3 / 60 (5.00%)	1 / 57 (1.75%)	3 / 57 (5.26%)
occurrences (all)	7	1	6
Nasal congestion			
subjects affected / exposed	6 / 60 (10.00%)	5 / 57 (8.77%)	5 / 57 (8.77%)
occurrences (all)	8	9	8
Nasal discomfort			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	4 / 60 (6.67%)	4 / 57 (7.02%)	6 / 57 (10.53%)
occurrences (all)	7	7	7
Productive cough			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	0	1	1
Pulmonary congestion			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Rhinitis allergic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	3
Rhinorrhoea			
subjects affected / exposed	1 / 60 (1.67%)	6 / 57 (10.53%)	4 / 57 (7.02%)
occurrences (all)	1	8	7
Sinus congestion			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	0	2	1
Sneezing			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Throat irritation			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	1	0	2
Upper respiratory tract congestion			
subjects affected / exposed	0 / 60 (0.00%)	2 / 57 (3.51%)	0 / 57 (0.00%)
occurrences (all)	0	2	0
Wheezing			

subjects affected / exposed	2 / 60 (3.33%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	4	1	0
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	1	0	1
Aggression			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Agitation			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	3	0	1
Anger			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	2 / 57 (3.51%)
occurrences (all)	0	2	2
Attention deficit/hyperactivity disorder			
subjects affected / exposed	3 / 60 (5.00%)	0 / 57 (0.00%)	2 / 57 (3.51%)
occurrences (all)	3	0	2
Depression			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Emotional disorder			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Encopresis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Initial insomnia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Insomnia			

subjects affected / exposed	0 / 60 (0.00%)	2 / 57 (3.51%)	0 / 57 (0.00%)
occurrences (all)	0	3	0
Mood swings			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Obsessive-compulsive disorder			
subjects affected / exposed	1 / 60 (1.67%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	1	1	0
Oppositional defiant disorder			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Sleep disorder			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Somnambulism			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Stress			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Tic			
subjects affected / exposed	1 / 60 (1.67%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	1	2	0
Investigations			
Blood aldosterone increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Blood bicarbonate abnormal			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0

Blood calcium increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Blood magnesium increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Blood pressure increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Immunoglobulins decreased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Renin increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Thyroxine free increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Thyroxine increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Urine colour abnormal			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	0	3	1
Weight decreased			
subjects affected / exposed	5 / 60 (8.33%)	1 / 57 (1.75%)	6 / 57 (10.53%)
occurrences (all)	5	1	6
Weight increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Accidental overdose			

subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Arthropod bite			
subjects affected / exposed	1 / 60 (1.67%)	3 / 57 (5.26%)	1 / 57 (1.75%)
occurrences (all)	1	3	2
Arthropod sting			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Back injury			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	8 / 60 (13.33%)	4 / 57 (7.02%)	8 / 57 (14.04%)
occurrences (all)	9	4	10
Chillblains			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	2
Excoriation			
subjects affected / exposed	3 / 60 (5.00%)	4 / 57 (7.02%)	0 / 57 (0.00%)
occurrences (all)	3	6	0
Eye injury			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Face injury			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	7 / 60 (11.67%)	7 / 57 (12.28%)	11 / 57 (19.30%)
occurrences (all)	14	7	15
Femur fracture			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	2	0
Foot fracture			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Hand fracture			

subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Head injury			
subjects affected / exposed	2 / 60 (3.33%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	3	0	0
Humerus fracture			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Iliotibial band syndrome			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Incision site erythema			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	1	0	1
Joint injury			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	5 / 57 (8.77%)
occurrences (all)	0	1	5
Joint sprain			
subjects affected / exposed	4 / 60 (6.67%)	1 / 57 (1.75%)	4 / 57 (7.02%)
occurrences (all)	4	1	4
Laceration			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	2	0	0
Limb injury			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	5 / 57 (8.77%)
occurrences (all)	0	1	6
Lower limb fracture			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Lumbar vertebral fracture			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Muscle strain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Post procedural discomfort			

subjects affected / exposed	3 / 60 (5.00%)	0 / 57 (0.00%)	6 / 57 (10.53%)
occurrences (all)	3	0	8
Post procedural haematoma			
subjects affected / exposed	4 / 60 (6.67%)	2 / 57 (3.51%)	3 / 57 (5.26%)
occurrences (all)	4	2	3
Post procedural swelling			
subjects affected / exposed	1 / 60 (1.67%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	1	1	0
Procedural pain			
subjects affected / exposed	11 / 60 (18.33%)	10 / 57 (17.54%)	10 / 57 (17.54%)
occurrences (all)	17	14	13
Scratch			
subjects affected / exposed	1 / 60 (1.67%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	1	1	0
Skin laceration			
subjects affected / exposed	0 / 60 (0.00%)	3 / 57 (5.26%)	0 / 57 (0.00%)
occurrences (all)	0	3	0
Spinal compression fracture			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	2
Sunburn			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Suture rupture			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Thermal burn			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Tibia fracture			
subjects affected / exposed	0 / 60 (0.00%)	2 / 57 (3.51%)	0 / 57 (0.00%)
occurrences (all)	0	2	0
Tooth fracture			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Tooth injury			

subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Traumatic haematoma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Wound			
subjects affected / exposed	2 / 60 (3.33%)	2 / 57 (3.51%)	0 / 57 (0.00%)
occurrences (all)	2	2	0
Wound dehiscence			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	0	1	1
Wrist fracture			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
Kidney malformation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Macroglossia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Dilatation ventricular			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	0	1	1
Left ventricular hypertrophy			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Palpitations			
subjects affected / exposed	2 / 60 (3.33%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	2	1	1
Sinus bradycardia			

subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Supraventricular extrasystoles			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Supraventricular tachycardia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Areflexia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Convulsion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	3 / 60 (5.00%)	4 / 57 (7.02%)	3 / 57 (5.26%)
occurrences (all)	3	5	4
Headache			
subjects affected / exposed	16 / 60 (26.67%)	14 / 57 (24.56%)	23 / 57 (40.35%)
occurrences (all)	85	25	69
Hypertonia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Hypotonia			
subjects affected / exposed	2 / 60 (3.33%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	2	0	1
Lethargy			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	1	0	1
Migraine			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	2 / 57 (3.51%)
occurrences (all)	2	0	4
Psychomotor hyperactivity			
subjects affected / exposed	1 / 60 (1.67%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	1	1	0

Sinus headache			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Unresponsive to stimuli			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 60 (0.00%)	2 / 57 (3.51%)	2 / 57 (3.51%)
occurrences (all)	0	2	2
Microcytic anaemia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear congestion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	2 / 57 (3.51%)
occurrences (all)	0	0	2
Ear pain			
subjects affected / exposed	1 / 60 (1.67%)	3 / 57 (5.26%)	2 / 57 (3.51%)
occurrences (all)	1	3	3
Motion sickness			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Tinnitus			
subjects affected / exposed	0 / 60 (0.00%)	2 / 57 (3.51%)	0 / 57 (0.00%)
occurrences (all)	0	2	0
Tympanic membrane hyperaemia			
subjects affected / exposed	2 / 60 (3.33%)	1 / 57 (1.75%)	2 / 57 (3.51%)
occurrences (all)	2	1	5
Tympanic membrane perforation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Eye disorders			

Abnormal sensation in eye			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Cataract			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	3 / 60 (5.00%)	1 / 57 (1.75%)	2 / 57 (3.51%)
occurrences (all)	3	1	2
Conjunctivitis allergic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Eye pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Eye pruritus			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Eye swelling			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	0	1	1
Eyelid cyst			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Hypermetropia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Ocular hyperaemia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	1	0	1
Vision blurred			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Visual impairment			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0

Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	2 / 60 (3.33%)	4 / 57 (7.02%)	0 / 57 (0.00%)
occurrences (all)	2	4	0
Abdominal pain			
subjects affected / exposed	12 / 60 (20.00%)	4 / 57 (7.02%)	8 / 57 (14.04%)
occurrences (all)	23	10	8
Abdominal pain lower			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	13 / 60 (21.67%)	9 / 57 (15.79%)	9 / 57 (15.79%)
occurrences (all)	32	13	18
Abdominal tenderness			
subjects affected / exposed	2 / 60 (3.33%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	2	1	0
Aerophagia			
subjects affected / exposed	1 / 60 (1.67%)	2 / 57 (3.51%)	1 / 57 (1.75%)
occurrences (all)	1	2	1
Anal pruritus			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Aphthous stomatitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Chapped lips			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	4 / 60 (6.67%)	2 / 57 (3.51%)	2 / 57 (3.51%)
occurrences (all)	6	2	3
Diarrhoea			
subjects affected / exposed	18 / 60 (30.00%)	15 / 57 (26.32%)	11 / 57 (19.30%)
occurrences (all)	39	20	15
Dyspepsia			

subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Enteritis			
subjects affected / exposed	2 / 60 (3.33%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	2	1	0
Faecal incontinence			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	1	0	1
Flatulence			
subjects affected / exposed	10 / 60 (16.67%)	4 / 57 (7.02%)	5 / 57 (8.77%)
occurrences (all)	10	4	5
Frequent bowel movements			
subjects affected / exposed	1 / 60 (1.67%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	1	1	0
Gastritis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Gingival bleeding			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Gingivitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Haematemesis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Ileus			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Lip dry			

subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Mouth ulceration			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	10 / 60 (16.67%)	7 / 57 (12.28%)	8 / 57 (14.04%)
occurrences (all)	16	9	16
Oral pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Reflux oesophagitis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Regurgitation			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	2 / 57 (3.51%)
occurrences (all)	1	0	4
Stomach discomfort			
subjects affected / exposed	5 / 60 (8.33%)	0 / 57 (0.00%)	4 / 57 (7.02%)
occurrences (all)	7	0	4
Tooth disorder			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Tooth impacted			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Tooth loss			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	1 / 60 (1.67%)	1 / 57 (1.75%)	2 / 57 (3.51%)
occurrences (all)	1	1	2
Vomiting			
subjects affected / exposed	28 / 60 (46.67%)	22 / 57 (38.60%)	33 / 57 (57.89%)
occurrences (all)	72	48	88
Skin and subcutaneous tissue disorders			

Acne			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Dermatitis allergic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Dermatitis contact			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	1	0	1
Dry skin			
subjects affected / exposed	0 / 60 (0.00%)	3 / 57 (5.26%)	2 / 57 (3.51%)
occurrences (all)	0	3	2
Ecchymosis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	2 / 60 (3.33%)	2 / 57 (3.51%)	1 / 57 (1.75%)
occurrences (all)	3	2	1
Erythema			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	3 / 57 (5.26%)
occurrences (all)	1	0	4
Exfoliative rash			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Heat rash			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Hyperkeratosis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0

Ingrowing nail			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	0	1	1
Keratosis pilaris			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Nail disorder			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Night sweats			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 60 (0.00%)	2 / 57 (3.51%)	0 / 57 (0.00%)
occurrences (all)	0	2	0
Rash			
subjects affected / exposed	8 / 60 (13.33%)	5 / 57 (8.77%)	6 / 57 (10.53%)
occurrences (all)	8	6	7
Rash erythematous			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Rash follicular			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Rash generalised			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	0	1	1
Rash papular			
subjects affected / exposed	2 / 60 (3.33%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	2	1	0
Scar			
subjects affected / exposed	5 / 60 (8.33%)	4 / 57 (7.02%)	4 / 57 (7.02%)
occurrences (all)	9	7	8

Skin discolouration			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Skin irritation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Skin lesion			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	0	1	1
Urticaria			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	0	1	1
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 60 (1.67%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	1	1	1
Enuresis			
subjects affected / exposed	3 / 60 (5.00%)	0 / 57 (0.00%)	4 / 57 (7.02%)
occurrences (all)	4	0	4
Incontinence			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Myoglobinuria			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	1	0	3
Pollakiuria			
subjects affected / exposed	2 / 60 (3.33%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	2	1	1
Pyelocaliectasis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	0	1	1
Renal cyst			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	0	1	1
Residual urine			

subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Strangury			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Ureteric dilatation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	2 / 60 (3.33%)	2 / 57 (3.51%)	2 / 57 (3.51%)
occurrences (all)	2	2	2
Urine abnormality			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 60 (11.67%)	2 / 57 (3.51%)	2 / 57 (3.51%)
occurrences (all)	9	2	2
Back pain			
subjects affected / exposed	6 / 60 (10.00%)	5 / 57 (8.77%)	9 / 57 (15.79%)
occurrences (all)	15	10	9
Coccydynia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Groin pain			
subjects affected / exposed	0 / 60 (0.00%)	2 / 57 (3.51%)	0 / 57 (0.00%)
occurrences (all)	0	3	0
Joint contracture			
subjects affected / exposed	3 / 60 (5.00%)	0 / 57 (0.00%)	3 / 57 (5.26%)
occurrences (all)	3	0	3
Joint swelling			

subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Lordosis			
subjects affected / exposed	2 / 60 (3.33%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	2	1	0
Muscle contracture			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	1 / 60 (1.67%)	5 / 57 (8.77%)	3 / 57 (5.26%)
occurrences (all)	1	8	4
Muscle tightness			
subjects affected / exposed	1 / 60 (1.67%)	1 / 57 (1.75%)	2 / 57 (3.51%)
occurrences (all)	1	1	2
Muscular weakness			
subjects affected / exposed	5 / 60 (8.33%)	2 / 57 (3.51%)	3 / 57 (5.26%)
occurrences (all)	5	2	3
Musculoskeletal chest pain			
subjects affected / exposed	1 / 60 (1.67%)	1 / 57 (1.75%)	2 / 57 (3.51%)
occurrences (all)	1	1	4
Musculoskeletal pain			
subjects affected / exposed	2 / 60 (3.33%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	2	1	1
Myalgia			
subjects affected / exposed	2 / 60 (3.33%)	2 / 57 (3.51%)	3 / 57 (5.26%)
occurrences (all)	2	2	3
Neck pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	1	0	1
Osteoporosis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	8 / 60 (13.33%)	6 / 57 (10.53%)	8 / 57 (14.04%)
occurrences (all)	16	7	12
Scoliosis			

subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Tendinous contracture			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Tendon disorder			
subjects affected / exposed	1 / 60 (1.67%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	1	1	1
Trendelenburg's symptom			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	2	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 60 (0.00%)	5 / 57 (8.77%)	2 / 57 (3.51%)
occurrences (all)	0	5	2
Catheter site infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Croup infectious			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	4 / 60 (6.67%)	4 / 57 (7.02%)	3 / 57 (5.26%)
occurrences (all)	5	4	4
Eczema infected			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Enterobiasis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	1	0	1
Eyelid infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0

Fungal infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	6 / 60 (10.00%)	4 / 57 (7.02%)	10 / 57 (17.54%)
occurrences (all)	7	7	10
Gastroenteritis viral			
subjects affected / exposed	3 / 60 (5.00%)	3 / 57 (5.26%)	4 / 57 (7.02%)
occurrences (all)	3	4	4
Genital candidiasis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	0 / 60 (0.00%)	2 / 57 (3.51%)	0 / 57 (0.00%)
occurrences (all)	0	2	0
Hordeolum			
subjects affected / exposed	2 / 60 (3.33%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	4	0	0
Influenza			
subjects affected / exposed	7 / 60 (11.67%)	8 / 57 (14.04%)	6 / 57 (10.53%)
occurrences (all)	9	9	8
Infusion site infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Lice infestation			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Localised infection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	1 / 60 (1.67%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	1	1	1
Measles			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1

Molluscum contagiosum			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	2 / 57 (3.51%)
occurrences (all)	1	0	3
Nasopharyngitis			
subjects affected / exposed	10 / 60 (16.67%)	13 / 57 (22.81%)	13 / 57 (22.81%)
occurrences (all)	15	17	22
Oral candidiasis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	2	0	0
Oral herpes			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Otitis externa			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	0	1	1
Otitis media			
subjects affected / exposed	2 / 60 (3.33%)	4 / 57 (7.02%)	0 / 57 (0.00%)
occurrences (all)	2	4	0
Paronychia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	4 / 57 (7.02%)
occurrences (all)	0	1	4
Pharyngitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	2 / 57 (3.51%)
occurrences (all)	0	0	2
Pharyngitis streptococcal			
subjects affected / exposed	2 / 60 (3.33%)	3 / 57 (5.26%)	1 / 57 (1.75%)
occurrences (all)	3	3	3
Pharyngotonsillitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	1 / 57 (1.75%)
occurrences (all)	0	1	1
Post procedural infection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0

Postoperative wound infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	3	0	0
Rhinitis			
subjects affected / exposed	3 / 60 (5.00%)	2 / 57 (3.51%)	7 / 57 (12.28%)
occurrences (all)	4	2	11
Roseola			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Scarlet fever			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	2 / 60 (3.33%)	4 / 57 (7.02%)	1 / 57 (1.75%)
occurrences (all)	2	7	1
Skin infection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Tinea capitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Tinea infection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Tinea pedis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	1	4	0
Tonsillitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	2 / 57 (3.51%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	12 / 60 (20.00%)	12 / 57 (21.05%)	9 / 57 (15.79%)
occurrences (all)	18	17	16

Urinary tract infection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Varicella			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	2 / 57 (3.51%)
occurrences (all)	0	1	2
Viral infection			
subjects affected / exposed	3 / 60 (5.00%)	1 / 57 (1.75%)	3 / 57 (5.26%)
occurrences (all)	4	1	3
Viral pharyngitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 60 (3.33%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	2	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 60 (8.33%)	2 / 57 (3.51%)	5 / 57 (8.77%)
occurrences (all)	6	2	6
Dehydration			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Hyperuricaemia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 57 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Iron deficiency			
subjects affected / exposed	0 / 60 (0.00%)	1 / 57 (1.75%)	0 / 57 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 December 2007	The changes implemented with this amendment are: - Information resulting from in vivo general toxicology studies of ataluren dosing for one month in mice was updated; - Information resulting from in vitro studies of human cytochrome P450 inhibition and induction was updated.
28 April 2008	The changes implemented with this amendment are: - Clarified that muscle dystrophin levels may be absent or reduced in Duchenne/Becker muscular dystrophy (DBMD) participants; - Clarified the required phenotypic evidence of DBMD by 9 years of age to ensure the enrollment of only BMD participants with more severe disease presentation and thereby limit the potential for a ceiling effect associated with the study-related efficacy evaluations; - Removed plasma renin as a laboratory parameter for potential exclusion from the study; - Clarified the duration of the follow-up period (that is, 6 weeks) requiring the use of contraceptives for sexually active participants; - Clarified the information regarding the metabolism of losartan by CYP2C9; - Clarified that participants must not use assistive devices during the 6MWD; - Clarified that blood pressure values collected during the 6MWD were not to be reconciled with blood pressure values collected with vital signs; - Clarified the wording to describe the methods used by the participants to complete the timed-function test (TFT) for running or walking 10 meters and climbing/descending stairs; - Clarified the wording to describe the documentation of the active heart rate during the 6MWD; - Clarified the site adverse event reporting requirements and de-identification of submitted source documentation to facilitate appropriate reporting by the sites; - Added and clarified assessments of 6MWD variability for upward adaption of sample size if variability was higher than expected; - Added a sensitivity analysis to determine the influence of assigning siblings to the same treatment group on the primary analysis; - Clarified the time-to-event analyses with regards to censoring; - Added a definition of treatment-emergent adverse events to clarify the safety analysis; - Corrected the number of participants for the interim efficacy and safety analysis from 100 to 90 participants (completing at least 24 weeks of treatment).
27 October 2008	The changes implemented with this amendment are: - Updated the required screening laboratory values based on experience to date in the DBMD study population. Thus, this amendment modified the screening laboratory parameters to allow for the inclusion of participants with clinically insignificant laboratory abnormalities and avoid unnecessary participant blood collection for retesting; - Modified the safety monitoring parameters and actions to be taken consistent with the changes to the laboratory entry criteria. This change was made to avoid the burden of unnecessary blood collection to reassess clinically inconsequential Grade 1 laboratory findings in this pediatric study population; - Removed the table describing the safety profile of ataluren; - Addressed the need for additional language to be inserted into the informed consent document encouraging participants and parents/guardians to avoid discussion of study-related procedures and study drug except with medical professionals involved in the study or in the care of the participant.

04 March 2009	The changes implemented with this amendment are: - Clarified that a participant is only required to walk for ≥75 meters during the 6MWD at Screening for the purpose of determining study eligibility, and that distances <75 meters are allowed for subsequent 6MWTs; - Revised the analysis plan for data derived from the SAM based on input from experts, recent literature, and assessment of initial pre-treatment data; - Updated the baseline 6MWD stratification from <270 meters and ≥270 meters to <350 meters and ≥350 meters. Prior to study start, the estimated mean 6MWD for the study population was ~270 meters; however, early assessment of pre-treatment 6MWD data (including 47 participants at Screening and 20 participants at Baseline visit) showed a mean 6MWD of ~350-360 meters; - Clarified that an overdose of study drug is the administration of a study drug dose >2 times the highest intended total daily dose level for this protocol; - Clarified the procedures for confirming Grade 1 or minor laboratory abnormalities; - Clarified that information regarding prior use of cardiac drugs for congestive heart failure (CHF) prophylaxis/treatment was also to be collected; - Clarified the parameters being measured for hematology laboratory assessments; - Clarified that not all muscle samples were to be processed and immunostained for various sarcoglycans and dystroglycan; rather, select samples may be assessed, as permitted by sample availability and observed dystrophin expression; - Revised the analysis plan for the 6MWD. Because the magnitudes of the changes in 6MWD were likely to be related to the baseline 6MWD, and because the MMRM was likely to have greater power than the repeated-measures analysis of covariance (RANOVA), the MMRM was to be used rather than the RANOVA.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported