Clinical trial results:
A Phase 3 Efficacy and Safety Study of Ataluren in Patients With Nonsense Mutation Distrophinopathy

Summary

EudraCT number	2012-004527-20
Trial protocol	BE CZ SE GB DE IT ES PL FR
Global end of trial date	20 August 2015

Results information

Result version number	v1 (current)
This version publication date	02 August 2020
First version publication date	02 August 2020

Trial information

Trial identification

Sponsor protocol code	PTC124-GD-020-DMD

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01826487
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., +011 44 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)	Yes
EMA paediatric investigation plan number(s)	EMEA-000115-PIP01-07
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	23 September 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 August 2015
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 ability of ataluren to slow disease progression as assessed by ambulatory decline (decrease in 6-minute walk distance [6MWD]).

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	26 March 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	35 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 68
Country: Number of subjects enrolled	Spain: 22
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	Turkey: 16
Country: Number of subjects enrolled	Chile: 14
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	United Kingdom: 13
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Australia: 10
Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Sweden: 7
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Brazil: 5
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	Switzerland: 3
Country: Number of subjects enrolled	Czech Republic: 3
Country: Number of subjects enrolled	Israel: 3

Worldwide total number of subjects	230
EEA total number of subjects	100

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)	209
Adolescents (12-17 years)	21
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 291 participants were screened for eligibility, of which 61 participants did not meet entry criteria.

Pre-assignment

Screening details:

A total of 230 eligible participants were randomized in 1:1 ratio to receive either placebo or ataluren. 2 participants, 1 in each treatment arm, were excluded from intent-to-treat (ITT) population; as they did not have at least 1 valid post-baseline 6MWD value, a requirement for inclusion in ITT population.

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	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo matched to ataluren orally 3 times a day (TID) at morning, midday, and evening for 48 weeks.

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

Dosage and administration details:

Placebo matched to ataluren will be administered as per the schedule specified in the arm.

Arm title	Ataluren

Arm description:

Participants received ataluren suspension orally TID, 10 milligrams/kilogram (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 will be administered as per the dose and schedule specified in the arm.

Number of subjects in period 1	Placebo	Ataluren
Started	115	115
As-treated Population	115	115
ITT Population	114	114
Completed	111	110
Not completed	4	5
Consent withdrawn by subject	1	3
Adverse event, non-fatal	1	1
Lost to follow-up	1	-
Protocol deviation	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matched to ataluren orally 3 times a day (TID) at morning, midday, and evening for 48 weeks.	
Reporting group title	Ataluren
Reporting group description:	
Participants received ataluren suspension orally TID, 10 milligrams/kilogram (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 values	Placebo	Ataluren	Total
Number of subjects	115	115	230
Age categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	9.0	8.9	
standard deviation	± 1.65	± 1.79	-
Sex: Female, Male			
Units: Subjects			
Female	0	0	0
Male	115	115	230
Baseline 6MWD			
The 6MWD test is a non-encouraged test performed in a 30 meters long flat corridor, where the participant is 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: Subjects			
<300 meters	22	25	47
>=300 to <400 meters	52	47	99
>=400 meters	41	43	84
6MWD			
6MWD test is a non-encouraged test performed in a 30 meters long flat corridor, where the participant is 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	362.69	364.04	
standard deviation	± 81.424	± 73.342	-
Time to Walk/Run 10 Meters			
Units: seconds			
arithmetic mean	6.83	6.66	
standard deviation	± 2.924	± 3.078	-
Time to Climb 4 Stairs			
Number of participants analyzed were 112 for each arm.			
Units: seconds			
arithmetic mean	6.76	5.99	

standard deviation	± 7.287	± 5.347	-
Time to Descend 4 Stairs			
Number of participants analyzed were 109 and 112 for Placebo and Ataluren arm respectively.			
Units: seconds			
arithmetic mean	5.05	5.07	
standard deviation	± 5.362	± 5.157	-
Physical Function Total Score as Measured by North Star Ambulatory Assessment (NSAA)			
Number of participants analyzed were 114 for each arm.			
Units: units on a scale			
arithmetic mean	60.2	60.9	
standard deviation	± 18.37	± 17.97	-
Pediatric Outcomes Data Collection Instrument (PODCI) Transfers/Basic Mobility Score			
PODCI includes a Global Functioning Scale and 5 core scales: Upper Extremity & Physical Function,Transfer/Basic Mobility, Sports/Physical Functioning, Pain/Comfort,and Happiness. Transfers/Basic Mobility domain assesses difficulty experienced in performing routine motor activities in daily life. Each domain was scored from 0 (poor outcome/worse health) to 100(the highest level of functioning & least pain). Number of participants analyzed were 114 for each arm.			
Units: units on a scale			
arithmetic mean	81.4	83.9	
standard deviation	± 15.79	± 13.10	-
Pediatric Outcomes Data Collection Instrument (PODCI) Sports/Physical Functioning Score			
PODCI includes a Global Functioning Scale and 5 core scales: Upper Extremity & Physical Function,Transfer/Basic Mobility, Sports/Physical Functioning, Pain/Comfort,and Happiness. Sports/Physical Functioning domain assesses difficulty encountered in participating in more active recreational activities. Each domain was scored from 0 (poor outcome/worse health) to 100(the highest level of functioning & least pain). Number of participants analyzed were 114 for each arm.			
Units: units on a scale			
arithmetic mean	56.0	56.2	
standard deviation	± 20.94	± 18.94	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo matched to ataluren orally 3 times a day (TID) at morning, midday, and evening for 48 weeks.	
Reporting group title	Ataluren
Reporting group description:	
Participants received ataluren suspension orally TID, 10 milligrams/kilogram (mg/kg) at morning, 10 mg/kg at midday, and 20 mg/kg at evening (total daily dose 40 mg/kg) 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 is a non-encouraged test performed in a 30 meters long flat corridor, where the participant is 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. Participants with confirmed loss of ambulation at a particular visit were assigned a 6MWD result of 0. Baseline and Week 48 6MWD values are each the average of two valid 6MWD values, or a single available value if one was missing. 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. Multiple imputation was applied to impute missing values within the treatment groups.	
End point type	Primary
End point timeframe:	
Baseline, Week 48	

End point values	Placebo	Ataluren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	114		
Units: meters				
least squares mean (standard error)	-60.67 (± 9.323)	-47.69 (± 9.247)		

Statistical analyses

Statistical analysis title	Placebo versus Ataluren
Statistical analysis description:	
Analysis was performed using analysis of covariance (ANCOVA) method including stratification factors for age (less than [<] 9 years versus [vs.] greater than or equal to [>=] 9 years), duration of use of corticosteroids at baseline (approx. >=6 to <12 months vs. >=12 months), and baseline 6MWD category (>=350 meters vs <350 meters), as well as baseline 6MWD as covariate.	
Comparison groups	Placebo v Ataluren

Number of subjects included in analysis	228
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.213 [1]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	12.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.44
upper limit	33.39
Variability estimate	Standard error of the mean
Dispersion value	10.415

Notes:

[1] - Threshold for significance at 0.05. Secondary endpoints were tested for significance, only if the primary endpoint was statistically significant.

Secondary: Time to 10 Percent (%) Persistent Worsening in 6MWD

End point title	Time to 10 Percent (%) Persistent Worsening in 6MWD

End point description:

6MWD test was performed in a 30 meters long flat corridor, where participant was instructed to walk as far as possible, back and forth around two cones, with permission to slow down, rest, or stop. Participants were not permitted to use assistive devices (walker, long leg braces, or short leg braces) during test. Time to 10% persistent worsening in 6MWD: last time that 6MWD was not 10% worse than baseline. For participants who did not have 10% 6MWD worsening or who were removed from study, time to 10% 6MWD worsening was censored at the time of last 6MWD test. Participants who became non-ambulatory were considered to have 10% worsening. 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. Multiple imputation was applied to impute missing value. 'n'=participants evaluable for specified categories. '99999'=data not calculated due to smaller number of participant with an event.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	Placebo	Ataluren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	114		
Units: days				
median (confidence interval 95%)				
<300 meters (n=21,24)	56 (1.0 to 111.0)	164 (1.0 to 225.0)		
>=300 to <400 meters (n=52,47)	280 (169.0 to 99999)	99999 (280.0 to 99999)		
>=400 meters (n=41,43)	99999 (99999 to 99999)	99999 (99999 to 99999)		

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:

The method of walk/run used by participant was categorized as follows: 1. Unable to walk independently; 2. Unable to walk independently but can walk with support; 3. Highly adapted gait, wide-based lordotic gait, cannot increase walking speed; 4. Moderately adapted gait, can pick up speed but cannot run; 5. Able to pick up speed but runs with a double stance phase (that is, cannot achieve both feet off the ground); 6. Runs and gets both feet off the ground (with no double stance phase). If time taken to perform a test exceeded 30 seconds or if a participant could not perform test due to disease progression, a value of 30 seconds was used. A cumulative 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, 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Placebo	Ataluren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	109		
Units: seconds				
arithmetic mean (standard deviation)	3.47 (± 6.393)	2.27 (± 5.216)		

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:

The method of climbing used by participant was categorized as follows: 1. Unable to up climb 4 standard stairs; 2. Climbs 4 standard stairs "marking time" (climbs one foot at a time, with both feet on a step before moving to next step), using both arms on one or both handrails; 3. Climbs 4 standard stairs "marking time" (climbs one foot at a time, with both feet on a step before moving to next step), using one arm on one handrail; 4. Climbs 4 standard stairs "marking time", not needing handrail; 5. Climbs 4 standard stairs alternating feet, needs handrail for support; 6. Climbs 4 standard stairs alternating feet, not needing handrail support. A cumulative 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, 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Placebo	Ataluren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	105		
Units: seconds				
arithmetic mean (standard deviation)	4.46 (± 7.310)	2.65 (± 5.297)		

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:

The method of descending used by participant was categorized as follows: 1. Unable to descend 4 standard stairs; 2. Descends 4 standard stairs "marking time" (climbs one foot at a time, with both feet on a step before moving to next step), using both arms on one or both handrails; 3. Descends 4 standard stairs "marking time", using one arm on one handrail; 4. Descends 4 standard stairs "marking time" (climbs one foot at a time, with both feet on a step before moving to next step), not needing handrail; 5. Descends 4 standard stairs alternating feet, needs handrail for support; 6. Descends 4 standard stairs alternating feet, not needing handrail support. A cumulative 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, 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Placebo	Ataluren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	106		
Units: seconds				
arithmetic mean (standard deviation)	3.97 (± 7.854)	2.15 (± 5.306)		

Statistical analyses

No statistical analyses for this end point

Secondary: 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	Secondary

End point timeframe:

Baseline up to Week 54

End point values	Placebo	Ataluren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	115		
Units: percentage of participants				
number (not applicable)	87.8	89.6		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Participants With Change From Baseline in Activities of Daily Living and Disease Status at Week 48, as Assessed by a Standardized Survey Administered by Site Personnel

End point title	Number of Participants With Change From Baseline in Activities of Daily Living and Disease Status at Week 48, as Assessed by a Standardized Survey Administered by Site Personnel

End point description:

At screening or baseline, participant and/or parent/caregiver were asked to identify any activities of daily living (ambulation, balance, personal hygiene/grooming, dressing and undressing, self-feeding, using bathroom, handwriting, school performance, behavior or energy level) or symptoms that were affected by participant's DMD. At post-baseline (Week 48), same participant and/or parent/caregiver was asked to describe any changes from baseline in those activities of daily living/symptoms, within following categories: physical functioning(PF); general energy level(EL); cognition/school function(C/SF); emotional/social functioning(E/SocF); and sleep. Changes were reported on a 5-point Likert scale:1=much worse,2=slightly worse,3=unchanged,4=slightly better, or 5=much better. 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 for specified categories.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 48

End point values	Placebo	Ataluren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	114		
Units: participants				
PF:Upper Extremity Activity-Much better (n=82,88)	1	4		
PF:Walking-Much better (n=112,108)	5	8		

PF:Climbing Stairs-Much better (n=105,110)	4	4		
PF:Other-Much better (n=65,68)	4	5		
C/SF-Much better (n=92,104)	6	5		
E/SocF-Much better (n=94,105)	3	8		
General EL-Much better (n=83,89)	3	8		
Sleep-Much better (n=85,91)	3	3		
Other-Much better (n=23,23)	0	1		
PF:Upper Extremity Activity-Slight better(n=82,88)	7	7		
PF:Walking-Slightly better (n=112,108)	13	16		
PF:Climbing Stairs-Slightly better (n=105,110)	8	13		
PF:Other-Slightly better (n=65,68)	9	10		
C/SF-Slightly better (n=92,104)	12	20		
E/SocF-Slightly better (n=94,105)	9	21		
General EL-Slightly better (n=83,89)	12	12		
Sleep-Slightly better (n=85,91)	4	8		
Other-Slightly better (n=23,23)	5	6		
PF:Upper Extremity Activity-Unchanged (n=82,88)	67	73		
PF:Walking-Unchanged (n=112,108)	57	60		
PF:Climbing Stairs-Unchanged (n=105,110)	61	65		
PF:Other-Unchanged (n=65,68)	38	44		
C/SF-Unchanged (n=92,104)	71	74		
E/SocF-Unchanged (n=94,105)	75	68		
General EL-Unchanged (n=83,89)	54	63		
Sleep-Unchanged (n=85,91)	73	76		
Other-Unchanged (n=23,23)	15	13		
PF:Upper Extremity Activity-Slight worse (n=82,88)	6	2		
PF:Walking-Slightly worse (n=112,108)	19	21		
PF:Climbing Stairs-Slightly worse (n=105,110)	17	15		
PF:Other-Slightly worse (n=65,68)	7	8		
C/SF-Slightly worse (n=92,104)	3	3		
E/SocF-Slightly worse (n=94,105)	5	6		
General EL-Slightly worse (n=83,89)	11	5		
Sleep-Slightly worse (n=85,91)	5	2		
Other-Slightly worse (n=23,23)	2	3		
PF:Upper Extremity Activity-Much worse (n=82,88)	1	2		
PF:Walking-Much worse (n=112,108)	18	3		
PF:Climbing Stairs-Much worse (n=105,110)	15	13		
PF:Other-Much worse (n=65,68)	7	1		
C/SF-Much worse (n=92,104)	0	2		
E/SocF-Much worse (n=94,105)	2	2		
General EL-Much worse (n=83,89)	3	1		
Sleep-Much worse (n=85,91)	0	2		
Other-Much worse (n=23,23)	1	0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Ataluren Plasma Concentration

End point title	Ataluren Plasma Concentration[2]

End point description:

Plasma samples for the determination of ataluren concentrations were analyzed using a validated high performance liquid chromatography with tandem mass spectrometry (HPLC/MS-MS) method with a lower limit of quantitation of 0.5 micrograms/milliliter (mcg/mL). As-treated population included all randomized participants who actually received any study treatment. Here, 'n' signifies participants evaluable at specified timepoint.

End point type	Other pre-specified

End point timeframe:

Weeks 8, 16, 24, 32, 40, and 48

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is reporting statistics for Ataluren arm only.

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	115			
Units: mcg/mL				
arithmetic mean (standard deviation)				
Week 08 (n=113)	4.230 (± 5.3913)			
Week 16 (n=113)	3.429 (± 3.9275)			
Week 24 (n=112)	3.323 (± 3.6135)			
Week 32 (n=113)	3.480 (± 3.1053)			
Week 40 (n=111)	3.997 (± 4.7615)			
Week 48 (n=110)	3.544 (± 3.8082)			

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 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	Placebo	Ataluren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	115		
Units: percentage of drug				
arithmetic mean (standard deviation)	95.1 (± 9.43)	95.7 (± 7.57)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Physical Function Total Score as Measured by NSAA at Week 48

End point title	Change From Baseline in Physical Function Total Score as Measured by NSAA at Week 48

End point description:

NSAA is a functional scale specifically designed for ambulant Duchenne muscular dystrophy (DMD) participants. It comprised tests for 17 abilities: ability to stand, rise from floor, get from lying to sitting, get from sitting to standing, raise one’s head, stand on one’s heels, hop, jump, and run. For each activity, a score of 0,1, or 2 was recorded, with 0=unable to achieve independently,1=modified method but achieves goal independently, or 2 =normal- achieves goal independently. Sum of these scores(except for 'raise one's head' activity) was reported as ordinal total score, which was transformed to a linear total score ranging from 0(worst) to 100(best). Participants with confirmed loss of ambulation at a particular visit were assigned a score of 0. 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. ‘Number of participants analyzed‘=participants evaluable for this endpoint.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 48

End point values	Placebo	Ataluren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	106		
Units: units on a scale				
arithmetic mean (standard deviation)	-8.4 (± 10.65)	-6.3 (± 10.64)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in PODCI Transfers/Basic Mobility and Sports/Physical Functioning Scores at Week 48

End point title	Change From Baseline in PODCI Transfers/Basic Mobility and Sports/Physical Functioning Scores at Week 48

End point description:

Changes in health-related quality of life(HRQL) were measured via PODCI questionnaire. PODCI includes a Global Functioning Scale and 5 core scales: Upper Extremity and Physical Function,Transfer/Basic Mobility, Sports/Physical Functioning, Pain/Comfort,and Happiness. Following PODCI domains were prespecified in protocol for analysis:Transfers/Basic Mobility domain assesses difficulty experienced in performing routine motor activities in daily life. Sports/Physical Functioning domain assesses difficulty encountered in participating in more active recreational activities. Each domain was scored from 0 to 100, with 0=poor outcome/worse health, while 100=the highest level of functioning and least pain. 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. 'Number of participants analyzed'=participants evaluable for this endpoint.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 48

End point values	Placebo	Ataluren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	109		
Units: units on a scale				
arithmetic mean (standard deviation)				
Transfers/Basic Mobility Score	-8.8 (± 15.80)	-6.6 (± 14.76)		
Sports/Physical Functioning Score	-7.3 (± 15.87)	-5.6 (± 15.91)		

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	15.1

Reporting groups	
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	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	Placebo	Ataluren	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 115 (3.48%)	4 / 115 (3.48%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Post-traumatic pain			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Myocarditis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Adenoidal hypertrophy			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal turbinate hypertrophy			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Tendon disorder			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Ataluren	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	99 / 115 (86.09%)	103 / 115 (89.57%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	
occurrences (all)	2	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	
occurrences (all)	2	1	
Hypotension			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Aortic dilatation			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Flushing			
subjects affected / exposed	3 / 115 (2.61%)	0 / 115 (0.00%)	
occurrences (all)	3	0	
Haematoma			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	12 / 115 (10.43%)	16 / 115 (13.91%)	
occurrences (all)	17	20	
Disease progression			

subjects affected / exposed	14 / 115 (12.17%)	9 / 115 (7.83%)	
occurrences (all)	15	9	
Abasia			
subjects affected / exposed	0 / 115 (0.00%)	3 / 115 (2.61%)	
occurrences (all)	0	3	
Oedema peripheral			
subjects affected / exposed	0 / 115 (0.00%)	3 / 115 (2.61%)	
occurrences (all)	0	3	
Fatigue			
subjects affected / exposed	3 / 115 (2.61%)	1 / 115 (0.87%)	
occurrences (all)	3	1	
Non-cardiac chest pain			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	
occurrences (all)	1	1	
Influenza like illness			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	
occurrences (all)	2	1	
Gait disturbance			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	3 / 115 (2.61%)	0 / 115 (0.00%)	
occurrences (all)	3	0	
Thirst			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Allergy to chemicals			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Seasonal allergy			
subjects affected / exposed	2 / 115 (1.74%)	2 / 115 (1.74%)	
occurrences (all)	2	2	
Rhinitis allergic			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	

Allergy to vaccine			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Drug hypersensitivity			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	
occurrences (all)	2	0	
Reproductive system and breast disorders			
Genital discomfort			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	13 / 115 (11.30%)	19 / 115 (16.52%)	
occurrences (all)	17	23	
Oropharyngeal pain			
subjects affected / exposed	6 / 115 (5.22%)	7 / 115 (6.09%)	
occurrences (all)	9	7	
Epistaxis			
subjects affected / exposed	4 / 115 (3.48%)	7 / 115 (6.09%)	
occurrences (all)	11	10	
Nasal congestion			
subjects affected / exposed	2 / 115 (1.74%)	3 / 115 (2.61%)	
occurrences (all)	3	5	
Rhinorrhoea			
subjects affected / exposed	3 / 115 (2.61%)	3 / 115 (2.61%)	
occurrences (all)	3	4	
Wheezing			
subjects affected / exposed	0 / 115 (0.00%)	3 / 115 (2.61%)	
occurrences (all)	0	3	
Asthmatic crisis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Productive cough			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Sneezing			

subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Sinus congestion			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	
occurrences (all)	3	0	
Sleep apnoea syndrome			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	
occurrences (all)	2	0	
Throat irritation			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Attention deficit/hyperactivity disorder			
subjects affected / exposed	1 / 115 (0.87%)	3 / 115 (2.61%)	
occurrences (all)	1	3	
Aggression			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	
occurrences (all)	0	2	
Sleep disorder			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	
occurrences (all)	0	3	
Abnormal behaviour			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Negativism			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Obsessive-compulsive disorder			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	
occurrences (all)	1	1	
Anxiety			

subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	
occurrences (all)	2	0	
Dysphemia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Middle insomnia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Mood swings			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	
occurrences (all)	2	0	
Investigations			
Renin increased			
subjects affected / exposed	3 / 115 (2.61%)	1 / 115 (0.87%)	
occurrences (all)	3	1	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	
occurrences (all)	0	2	
Arthropod sting			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	
occurrences (all)	1	1	
Concussion			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	20 / 115 (17.39%)	21 / 115 (18.26%)	
occurrences (all)	31	35	
Contusion			
subjects affected / exposed	4 / 115 (3.48%)	3 / 115 (2.61%)	
occurrences (all)	4	3	
Ligament sprain			
subjects affected / exposed	7 / 115 (6.09%)	3 / 115 (2.61%)	
occurrences (all)	7	3	
Laceration			

subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	
occurrences (all)	1	3	
Post-traumatic pain			
subjects affected / exposed	4 / 115 (3.48%)	2 / 115 (1.74%)	
occurrences (all)	5	2	
Spinal compression fracture			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	
occurrences (all)	1	2	
Electrical burn			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Excoriation			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	
occurrences (all)	1	1	
Fibula fracture			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Foot fracture			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	
occurrences (all)	1	1	
Hand fracture			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	
occurrences (all)	1	1	
Joint injury			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	
occurrences (all)	1	1	
Muscle injury			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Muscle strain			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Scratch			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	2	
Tibia fracture			

subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Tooth injury			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Ulna fracture			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Upper limb fracture			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Head injury			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Limb injury			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Lip injury			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Thermal burn			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	
occurrences (all)	2	0	
Cardiac disorders			
Right ventricular hypertrophy			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	
occurrences (all)	0	2	
Left ventricular dysfunction			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	2	
Left ventricular hypertrophy			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Myocardial fibrosis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	

Palpitations			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	
occurrences (all)	2	1	
Cardiomyopathy			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Wolff-Parkinson-White syndrome			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	21 / 115 (18.26%)	21 / 115 (18.26%)	
occurrences (all)	29	55	
Autism			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Coordination abnormal			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Epilepsy			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	
occurrences (all)	1	2	
Dizziness			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Hypotonia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Sinus headache			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	
occurrences (all)	0	2	
Petit mal epilepsy			

subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Psychomotor hyperactivity			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	
occurrences (all)	1	1	
Restless legs syndrome			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Splenomegaly			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Leukocytosis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Lymphadenopathy			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	4 / 115 (3.48%)	0 / 115 (0.00%)	
occurrences (all)	4	0	
Middle ear effusion			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Tympanic membrane disorder			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Eye disorders			

Astigmatism			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Cataract			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	
occurrences (all)	1	1	
Conjunctivitis			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	
occurrences (all)	2	0	
Eye allergy			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Conjunctivitis allergic			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Eye movement disorder			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Eyelid oedema			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Myopia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	10 / 115 (8.70%)	20 / 115 (17.39%)	
occurrences (all)	13	33	
Abdominal pain upper			
subjects affected / exposed	13 / 115 (11.30%)	9 / 115 (7.83%)	
occurrences (all)	17	9	
Abdominal pain			
subjects affected / exposed	5 / 115 (4.35%)	7 / 115 (6.09%)	
occurrences (all)	10	8	
Abdominal discomfort			

subjects affected / exposed	0 / 115 (0.00%)	3 / 115 (2.61%)	
occurrences (all)	0	4	
Constipation			
subjects affected / exposed	10 / 115 (8.70%)	3 / 115 (2.61%)	
occurrences (all)	12	4	
Flatulence			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	
occurrences (all)	1	2	
Abnormal faeces			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Breath odour			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Dental caries			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	2	
Dry mouth			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	
occurrences (all)	1	2	
Dyspepsia			
subjects affected / exposed	3 / 115 (2.61%)	1 / 115 (0.87%)	
occurrences (all)	3	1	
Gastritis			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	
occurrences (all)	1	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	
occurrences (all)	2	1	
Haemorrhoids			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	
occurrences (all)	1	1	
Anal fissure			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Food poisoning			

subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Haematochezia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Inguinal hernia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Irritable bowel syndrome			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	21 / 115 (18.26%)	26 / 115 (22.61%)	
occurrences (all)	26	44	
Nausea			
subjects affected / exposed	7 / 115 (6.09%)	7 / 115 (6.09%)	
occurrences (all)	8	7	
Tooth crowding			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	
occurrences (all)	0	2	
Malocclusion			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Odynophagia			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	2	
Oral pain			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Rectal haemorrhage			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	
occurrences (all)	2	0	
Swollen tongue			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Toothache			

subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Hepatic steatosis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Acne			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Dermatitis allergic			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	4 / 115 (3.48%)	4 / 115 (3.48%)	
occurrences (all)	5	6	
Ingrowing nail			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	
occurrences (all)	0	2	
Pruritus			
subjects affected / exposed	2 / 115 (1.74%)	2 / 115 (1.74%)	
occurrences (all)	2	2	
Rash erythematous			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	
occurrences (all)	1	2	
Dry skin			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Ecchymosis			

subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Hair texture abnormal			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Hirsutism			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Skin burning sensation			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Skin lesion			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Skin mass			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Erythema			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Skin exfoliation			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Skin hyperpigmentation			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 115 (0.87%)	7 / 115 (6.09%)	
occurrences (all)	1	7	
Dysuria			
subjects affected / exposed	3 / 115 (2.61%)	2 / 115 (1.74%)	
occurrences (all)	3	4	

Bladder trabeculation			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Enuresis			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	
occurrences (all)	1	4	
Flank pain			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Hypercalciuria			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Myoglobinuria			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Nephrolithiasis			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	
occurrences (all)	2	0	
Urinary incontinence			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	
occurrences (all)	1	2	
Polyuria			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Urine abnormality			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	
occurrences (all)	5	2	
Renal cyst			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Pollakiuria			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Hypothyroidism			

subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Hyperaldosteronism			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	8 / 115 (6.96%)	11 / 115 (9.57%)	
occurrences (all)	8	15	
Arthralgia			
subjects affected / exposed	5 / 115 (4.35%)	6 / 115 (5.22%)	
occurrences (all)	5	7	
Foot deformity			
subjects affected / exposed	2 / 115 (1.74%)	3 / 115 (2.61%)	
occurrences (all)	3	3	
Growing pains			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Bone pain			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	
occurrences (all)	2	0	
Pain in extremity			
subjects affected / exposed	14 / 115 (12.17%)	10 / 115 (8.70%)	
occurrences (all)	17	12	
Myalgia			
subjects affected / exposed	0 / 115 (0.00%)	3 / 115 (2.61%)	
occurrences (all)	0	4	
Musculoskeletal chest pain			
subjects affected / exposed	2 / 115 (1.74%)	2 / 115 (1.74%)	
occurrences (all)	2	3	
Musculoskeletal pain			
subjects affected / exposed	2 / 115 (1.74%)	2 / 115 (1.74%)	
occurrences (all)	2	2	
Joint contracture			

subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Muscle atrophy			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Muscle tightness			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Muscular weakness			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	
occurrences (all)	1	1	
Osteoporosis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Scoliosis			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	
occurrences (all)	2	1	
Tendinous contracture			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Joint crepitation			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Lordosis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Osteopenia			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Ear infection			
subjects affected / exposed	1 / 115 (0.87%)	6 / 115 (5.22%)	
occurrences (all)	1	8	

Gastroenteritis			
subjects affected / exposed	4 / 115 (3.48%)	5 / 115 (4.35%)	
occurrences (all)	4	7	
Influenza			
subjects affected / exposed	5 / 115 (4.35%)	3 / 115 (2.61%)	
occurrences (all)	8	4	
Bronchitis			
subjects affected / exposed	3 / 115 (2.61%)	2 / 115 (1.74%)	
occurrences (all)	3	2	
Conjunctivitis infective			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	
occurrences (all)	0	2	
Fungal skin infection			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	
occurrences (all)	1	4	
Gastroenteritis viral			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	
occurrences (all)	0	2	
Gastrointestinal viral infection			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	
occurrences (all)	0	3	
Hordeolum			
subjects affected / exposed	3 / 115 (2.61%)	2 / 115 (1.74%)	
occurrences (all)	3	3	
Eye infection			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	
occurrences (all)	1	1	
Gingivitis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	2	
Herpes simplex			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	2	
Lower respiratory tract infection			
subjects affected / exposed	4 / 115 (3.48%)	1 / 115 (0.87%)	
occurrences (all)	4	2	

Lung infection			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Acute tonsillitis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Adenoiditis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal infection			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	
occurrences (all)	2	0	
Gingival infection			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Helminthic infection			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Infected bites			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	22 / 115 (19.13%)	24 / 115 (20.87%)	
occurrences (all)	33	43	
Upper respiratory tract infection			
subjects affected / exposed	6 / 115 (5.22%)	11 / 115 (9.57%)	
occurrences (all)	11	16	
Rhinitis			
subjects affected / exposed	4 / 115 (3.48%)	8 / 115 (6.96%)	
occurrences (all)	4	13	
Pharyngitis			
subjects affected / exposed	4 / 115 (3.48%)	4 / 115 (3.48%)	
occurrences (all)	5	4	
Tonsillitis			
subjects affected / exposed	2 / 115 (1.74%)	3 / 115 (2.61%)	
occurrences (all)	3	3	

Sinusitis			
subjects affected / exposed	2 / 115 (1.74%)	5 / 115 (4.35%)	
occurrences (all)	2	6	
Viral infection			
subjects affected / exposed	3 / 115 (2.61%)	3 / 115 (2.61%)	
occurrences (all)	3	3	
Nail infection			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	
occurrences (all)	0	3	
Respiratory tract infection			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	
occurrences (all)	1	2	
Pneumonia			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	
occurrences (all)	0	2	
Otitis externa			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Otitis media			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	
occurrences (all)	3	1	
Parasitic gastroenteritis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Skin infection			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	
occurrences (all)	1	1	
Mycoplasma infection			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Oral candidiasis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Oral herpes			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	

Pharyngitis streptococcal			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Rubella			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Tracheitis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	3 / 115 (2.61%)	5 / 115 (4.35%)	
occurrences (all)	3	5	
Decreased appetite			
subjects affected / exposed	2 / 115 (1.74%)	3 / 115 (2.61%)	
occurrences (all)	2	3	
Electrolyte imbalance			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	
occurrences (all)	1	2	
Vitamin D deficiency			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	
occurrences (all)	0	2	
Abnormal weight gain			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	
occurrences (all)	1	1	
Dyslipidaemia			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Fluid retention			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	3	
Hypercholesterolaemia			

subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	
occurrences (all)	2	1	
Hyperlipidaemia			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	
occurrences (all)	1	1	
Iron deficiency			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences (all)	0	1	
Hyperglycaemia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Hyperkalaemia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Hyperuricaemia			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	
occurrences (all)	2	0	
Hypervitaminosis D			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Hypoglycaemia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Hyponatraemia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Increased appetite			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	
Metabolic acidosis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 June 2013	The changes implemented with this amendment are: - Incorporated feedback from the European Medicines Agency (EMA) related to the non-allowance of protocol waivers; - Added the timed test of rising from supine to stand; - Amended the criteria for withdrawal of a participant from the study due to the participant's condition substantially worsening after initiating study drug to include worsening of cardiac events such as QTc interval limits, new evidence of symptomatic cardiomyopathy, and significant decrease in left ventricular ejection fraction; - Deleted any requirement that there be any discussion between the investigator and the PTC Therapeutics medical monitor before unblinding a participant; Added information regarding benefits and risks of study participation.
04 March 2014	The changes implemented with this amendment are: - Updated information regarding ongoing ataluren studies; - Clarified inclusion criterion related to documentation of gene sequencing; - Clarified inclusion criterion related to no more than 20% change from screening to baseline 6MWD; - Updated the approximate number of investigator sites participating in study; - Updated the requirement for collection of date of birth for Screening; - Updated the actions to be taken in event of urine blood abnormalities; - Added information regarding renal abnormalities related to aminoglycosides; - Updated information regarding drugs metabolized by cytochrome P450 enzymes; - Updated information regarding potential drug interactions; - Updated schedule of events to clarify the timing of events such as randomization, study drug administration in clinic, study drug dispensing, and the Visit 2, Day 2 6MWT; - Updated the recommended sequence of study procedures at Visit 2 to 8, by updating sequence of events and timing of randomization; - Clarified the timing of randomization of a participant at Visit 2, Day 2; - Clarified End-of-Treatment Visit procedures for participants who discontinue prematurely; - Clarified Post-Treatment Visits procedures; - Added information regarding videotaping of the 6MWT, timed function tests, and NSAA; - Clarified the schedule for administration of Activities of Daily Living/Disease Symptom Survey at baseline; - Updated the blood volumes for the required blood draws; - Added information regarding blood pressure assessment; - Summarized information regarding tumor findings in rat studies as already included in the Ataluren Investigator Brochure; - Deleted any mention of forfeiture of participation in the open-label extension study for breaking the blind of the study; - Added information regarding benefits and risks of study participation.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported