



## Clinical trial results: An Open-Label Study for Previously Treated Ataluren (PTC124®) Patients with Nonsense Mutation Dystrophinopathy Summary

EudraCT number	2011-004853-18
Trial protocol	BE SE DE GB ES FR IT
Global end of trial date	19 January 2019

### Results information

Result version number	v1
This version publication date	18 October 2020
First version publication date	18 October 2020

### Trial information

#### Trial identification

Sponsor protocol code	PTC124-GD-019-DMD
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01557400
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	PTC Therapeutics, Inc.
Sponsor organisation address	100 Corporate Court, South Plainfield, United States, 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)	EMA-000115-PIP01-07
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 January 2018
Global end of trial reached?	Yes
Global end of trial date	19 January 2019
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary study objective was to assess the long-term safety and tolerability of a 10 milligrams/kilograms (mg/kg), 10 mg/kg, 20 mg/kg ataluren regimen in participants  $\geq 5$  years of age with nmDBMD who had prior exposure to ataluren in a PTC-sponsored clinical trial.

Protection of trial subjects:

The trial was conducted in accordance with Declaration of Helsinki in its revised edition (2013), and in conformance with the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guidance documents.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 May 2012
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	Australia: 9
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Canada: 12
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Israel: 10
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	Sweden: 8
Country: Number of subjects enrolled	United Kingdom: 19
Worldwide total number of subjects	94
EEA total number of subjects	63

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)	24
Adolescents (12-17 years)	65
Adults (18-64 years)	5
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The treatment gap between the date of administration of the last dose of ataluren in Study PTC124-GD-007-DMD (NCT00592553) and Study PTC124-GD-007e-DMD (NCT00847379) and the date of administration of the first dose of ataluren in this study (PTC124-GD-019-DMD) ranged from 114.43 to 266.14 weeks (801 to 1863 days).

### Pre-assignment

Screening details:

Of the 94 enrolled participants, 44 were not ambulatory and 84 were on concomitant therapy with corticosteroids. Participants who were non-ambulatory were not able to run/walk 10 meters in  $\leq 30$  seconds at study entry.

### Period 1

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

### Arms

Arm title	Ataluren
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Arm description:

Ataluren was provided as a vanilla-flavored powder to be mixed with water, milk, fruit juice (except apple juice) fruit punch, or in semi-solid food (for example, yogurt, pudding, or applesauce). The dose level for ataluren was 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening. Administration within 30 minutes after a meal was recommended. Study drug dosing was based on milligrams of drug per kilogram of body weight. Because of potential changes in participant body weight over time, weight-based dose adjustment occurred every 24 weeks as required. Study drug was taken for up to 240 weeks.

Arm type	Experimental
Investigational medicinal product name	Ataluren
Investigational medicinal product code	PTC124
Other name	
Pharmaceutical forms	Powder 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.

Number of subjects in period 1	Ataluren
Started	94
Received at Least 1 Dose of Study Drug	94
Completed	37
Not completed	57
Adverse event, serious fatal	2
Transitioned to Commercial Drug Product	40
Consent withdrawn by subject	9
Adverse event, non-fatal	1

Lost to follow-up	5
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## Baseline characteristics

### Reporting groups

Reporting group title	Ataluren
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Reporting group description:

Ataluren was provided as a vanilla-flavored powder to be mixed with water, milk, fruit juice (except apple juice) fruit punch, or in semi-solid food (for example, yogurt, pudding, or applesauce). The dose level for ataluren was 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening. Administration within 30 minutes after a meal was recommended. Study drug dosing was based on milligrams of drug per kilogram of body weight. Because of potential changes in participant body weight over time, weight-based dose adjustment occurred every 24 weeks as required. Study drug was taken for up to 240 weeks.

Reporting group values	Ataluren	Total	
Number of subjects	94	94	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	24	24	
Adolescents (12-17 years)	65	65	
Adults (18-64 years)	5	5	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	12.8		
standard deviation	± 2.38	-	
Sex: Female, Male			
Units: Subjects			
Female	0	0	
Male	94	94	
Race/Ethnicity, Customized			
Race data were collected, and ethnicity data were not collected in this study.			
Units: Subjects			
Caucasian	87	87	
Asian	4	4	
Other	2	2	
Unknown/Not Reported	1	1	
6-Minute Walk Distance (6MWD) as Measured by the 6-Minute Walk Test (6MWT)			
The 6MWD was assessed in participants who were ambulatory using standardized procedures. Participants were not permitted to use assistive devices (walker, long leg braces, or short leg braces) during the 6MWD test.			
Units: meters			
arithmetic mean	341.63		
standard deviation	± 108.106	-	

Physical Function as Measured by the North Star Ambulatory Assessment (NSAA)			
The NSAA was used to evaluate physical function in participants who were ambulatory at study entry, using standardized procedures. The NSAA consisted of 17 activities, each scored as 0, 1, or 2. The sum of these 17 scores was used to form a total score. If fewer than 13 of the 17 activities were performed, the total score was considered missing. If from 13 to 16 activities were performed, the total score was calculated by multiplying the sum of the scores in the x activities that were performed by 17/x. The linear score was the linear transformation of the NSAA score to a scale of 0 to 100.			
Units: units on a scale arithmetic mean standard deviation	19.1 ± 8.52	-	
Time to Stand From Supine Position			
Time to stand from the supine position to a standing position was assessed in ambulatory participants. If the time taken to perform a test exceeded 30 seconds, a value of 30 seconds was used.			
Units: seconds arithmetic mean standard deviation	18.56 ± 34.349	-	
Time to Walk/Run 10 Meters			
Time to walk/run 10 meters was measured in ambulatory participants. If the time taken to perform a test exceeded 30 seconds, a value of 30 seconds was used.			
Units: seconds arithmetic mean standard deviation	8.35 ± 4.693	-	
Percent-Predicted Forced Vital Capacity (FVC) as Measured by Spirometry			
Pulmonary function parameter of FVC was assessed in non-ambulatory participants by using a spirometer. Due to the difficulty in obtaining an accurate standing height measurement in non-ambulatory participants, ulna length and arm span were used as a surrogate measure for height when calculating percent-predicted FVC.			
Units: liters arithmetic mean standard deviation	1.94 ± 0.509	-	
Percent-Predicted Forced Expiratory Volume in 1 Second (FEV1) as Measured by Spirometry			
Pulmonary function parameter of FEV1 was assessed in non-ambulatory participants by using a spirometer.			
Units: liters arithmetic mean standard deviation	68.60 ± 18.295	-	
Peak Expiratory Flow (PEF) as Measured by Spirometry			
Pulmonary function parameter of PEF was assessed in non-ambulatory participants by using a spirometer.			
Units: liters arithmetic mean standard deviation	9.09 ± 34.350	-	
Peak Cough Flow (PCF) as Measured by Spirometry			
Pulmonary function parameter of peak cough flow (PCF) was assessed in non-ambulatory participants by using a spirometer.			
Units: liters arithmetic mean standard deviation	33.06 ± 81.985	-	
Participant and Parent/Caregiver-Reported Activities of Daily Living (ADL), as Measured by EK Scale			

Egen Klassifikation (EK scale): ordinal scale ranging from 0 (highest level of independent function)-30 (lowest level) points. Scale categories (each scored 0-3): 1) ability to use wheelchair, 2) ability to transfer from wheelchair, 3) ability to stand, 4) ability to balance in the wheelchair, 5) ability to move arms, 6) ability to use hands/arms when eating, 7) ability to turn in bed, 8) ability to cough, 9) ability to speak, and 10) physical well-being. Participant is interviewed to capture how he performs tasks of daily life (Categories 1-9) and how he perceives his wellbeing (Category 10).

Units: units on a scale			
arithmetic mean	7.8		
standard deviation	± 3.76	-	



## End points

### End points reporting groups

Reporting group title	Ataluren
Reporting group description:	
Ataluren was provided as a vanilla-flavored powder to be mixed with water, milk, fruit juice (except apple juice) fruit punch, or in semi-solid food (for example, yogurt, pudding, or applesauce). The dose level for ataluren was 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening. Administration within 30 minutes after a meal was recommended. Study drug dosing was based on milligrams of drug per kilogram of body weight. Because of potential changes in participant body weight over time, weight-based dose adjustment occurred every 24 weeks as required. Study drug was taken for up to 240 weeks.	

### Primary: Number of Participants With Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs) <sup>[1]</sup>
End point description:	
TEAE is any untoward medical occurrence or undesirable event(s) experienced in a participant that begins or worsens following administration of study drug, whether or not considered related to study drug by the Investigator. A serious adverse event (SAE) was an adverse event (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), or persistent or significant disability/incapacity not related to nmDBMD. AEs included both SAEs and non-serious AEs. AEs classified according to National Cancer Institute Common Terminology Criteria for Adverse Events version 3.0 (CTCAE) and coded using the Medical Dictionary for Regulatory Activities (MedDRA). A summary of serious and all other non-serious AEs, regardless of causality, is located in the Reported AEs module. Population included all enrolled participants who received at least 1 dose of study drug.	
End point type	Primary
End point timeframe:	
Baseline up to Week 246	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.	
Justification: Statistical analyses not applicable for this endpoint.	

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	94			
Units: participants				
TEAEs	91			
Treatment-Emergent SAEs	31			
TEAEs Related to Study Treatment	26			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in 6MWD as Measured by the 6MWT

End point title	Change From Baseline in 6MWD as Measured by the 6MWT
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End point description:

The 6MWD was assessed in participants who were ambulatory using standardized procedures. Participants were not permitted to use assistive devices (walker, long leg braces, or short leg braces) during the 6MWD test. Population included all enrolled participants who received at least 1 dose of study drug, were ambulatory, and had evaluable 6MWT data. Participants who were ambulatory were able to run/walk 10 meters in  $\leq 30$  seconds at study entry.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 48, 96, 144, 192, and 240

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: change in meters				
arithmetic mean (standard deviation)				
Week 48	-41.71 ( $\pm$ 48.172)			
Week 96	-76.80 ( $\pm$ 70.781)			
Week 144	-97.57 ( $\pm$ 83.761)			
Week 192	-109.37 ( $\pm$ 96.238)			
Week 240	-134.16 ( $\pm$ 94.716)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Physical Function as Measured by the NSAA

End point title	Change From Baseline in Physical Function as Measured by the NSAA
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End point description:

The NSAA was used to evaluate physical function in those participants who were ambulatory at study entry, using standardized procedures. The NSAA consisted of 17 activities, each scored as 0, 1, or 2. The sum of these 17 scores was used to form a total score. If fewer than 13 of the 17 activities were performed, the total score was considered missing. If from 13 to 16 activities were performed, the total score was calculated by multiplying the sum of the scores in the x activities that were performed by 17/x. If an activity could not be performed due to disease progression/loss of ambulation, a score of zero was assigned. The linear score was the linear transformation of the NSAA score to a scale of 0 to 100. Population included all enrolled participants who received at least 1 dose of study drug, were ambulatory, and had evaluable NSAA data. Participants who were ambulatory were able to run/walk 10 meters in  $\leq 30$  seconds at study entry.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 48, 96, 144, 192, and 240

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 48	-2.9 (± 3.08)			
Week 96	-7.4 (± 5.61)			
Week 144	-8.8 (± 6.29)			
Week 240	-13.4 (± 7.03)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Time to Stand From Supine Position

End point title	Change From Baseline in Time to Stand From Supine Position
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End point description:

Time to stand from the supine position to a standing position was assessed in ambulatory participants. If the time taken to perform a test exceeded 30 seconds or if a participant could not perform the test due to disease progression, a value of 30 seconds was used. Population included all enrolled participants who received at least 1 dose of study drug, were ambulatory, and had evaluable time to stand from supine data. Participants who were ambulatory were able to run/walk 10 meters in ≤30 seconds at study entry.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 48, 96, 144, 192, and 240

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: seconds				
arithmetic mean (standard deviation)				
Week 48	3.33 (± 5.390)			
Week 96	6.38 (± 6.029)			
Week 144	6.11 (± 6.798)			
Week 192	3.84 (± 8.410)			
Week 240	11.16 (± 10.718)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Time to Walk/Run 10 Meters

End point title	Change From Baseline in Time to Walk/Run 10 Meters
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**End point description:**

Time to walk/run 10 meters was measured in ambulatory participants. If the time taken to perform a test exceeded 30 seconds or if a participant could not perform the test due to disease progression, a value of 30 seconds was used. Population included all enrolled participants who received at least 1 dose of study drug, were ambulatory, and had evaluable data for time to walk/run 10 meters. Participants who were ambulatory were able to run/walk 10 meters in  $\leq 30$  seconds at study entry.

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End point type	Secondary
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**End point timeframe:**

Baseline, Weeks 48, 96, 144, 192, and 240

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End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: seconds				
arithmetic mean (standard deviation)				
Week 48	1.67 ( $\pm$ 1.957)			
Week 96	3.48 ( $\pm$ 4.481)			
Week 144	3.07 ( $\pm$ 2.092)			
Week 192	3.19 ( $\pm$ 2.049)			
Week 240	3.62 ( $\pm$ 1.858)			

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**Statistical analyses**

No statistical analyses for this end point

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**Secondary: Change From Baseline in Pulmonary Function as Measured by Spirometry**

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End point title	Change From Baseline in Pulmonary Function as Measured by Spirometry
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**End point description:**

Pulmonary function parameters of percent-predicated FVC, percent-predicted FEV1 (adjusted using ulna length and age), PEF, and PCF was assessed in non-ambulatory participants by using a spirometer. Due to the difficulty in obtaining an accurate standing height measurement in non-ambulatory participants, ulna length and arm span were used as a surrogate measure for height when calculating percent-predicted FVC. Population included all enrolled participants who received at least 1 dose of study drug, were non-ambulatory, and had evaluable spirometry data. Participants who were non-ambulatory were not able to run/walk 10 meters in  $\leq 30$  seconds at study entry.

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End point type	Secondary
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**End point timeframe:**

Baseline, Weeks 48, 96, 144, 192, and 240

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End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: liters				
arithmetic mean (standard deviation)				
FVC, Week 48	-0.00 (± 0.239)			
FVC, Week 96	-0.06 (± 0.391)			
FVC, Week 144	-0.18 (± 0.422)			
FVC, Week 192	-0.18 (± 0.760)			
FVC, Week 240	-0.24 (± 0.720)			
FEV1, Week 48	-7.98 (± 10.297)			
FEV1, Week 96	-11.59 (± 13.366)			
FEV1, Week 144	-20.60 (± 18.201)			
FEV1, Week 192	-19.72 (± 21.916)			
FEV1, Week 240	-29.17 (± 18.759)			
PEF, Week 48	-7.47 (± 40.552)			
PEF, Week 96	9.67 (± 78.591)			
PEF, Week 144	-8.34 (± 42.763)			
PEF, Week 192	-9.66 (± 45.356)			
PEF, Week 240	-23.77 (± 70.864)			
PCF, Week 48	-3.67 (± 63.604)			
PCF, Week 96	-14.34 (± 94.453)			
PCF, Week 144	-48.51 (± 102.197)			
PCF, Week 192	-52.19 (± 105.178)			
PCF, Week 240	-81.38 (± 123.517)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Participant and Parent/Caregiver-Reported ADL, as Measured by the EK Scale

End point title	Change From Baseline in Participant and Parent/Caregiver-Reported ADL, as Measured by the EK Scale
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End point description:

Activities of daily living measured using EK scale, ranging from 0 points (highest level of independent

function) to 30 points (lowest). Scale=10 categories (each scored 0-3) with following functional domains 1) ability to use wheelchair, 2) ability to transfer from wheelchair, 3) ability to stand, 4) ability to balance in wheelchair, 5) ability to move arms, 6) ability to use hands and arms when eating, 7) ability to turn in bed, 8) ability to cough, 9) ability to speak, 10) physical well-being. Administration of EK scale consisted of an interview of participant to capture how he performs tasks of daily life (described by Categories 1-9) and how he perceives his wellbeing (described by Category 10). The interviewer assigned final score. Population included all enrolled participants who received at least 1 dose of study drug, were non-ambulatory, and had evaluable EK scale data. Participants who were non-ambulatory were not able to run/walk 10 meters in ≤30 seconds at study entry.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 48, 96, 144, 192, and 240

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 48	2.0 (± 3.03)			
Week 96	2.6 (± 2.85)			
Week 144	3.3 (± 2.31)			
Week 192	5.3 (± 2.51)			
Week 240	7.0 (± 2.49)			

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 246

Assessment type	Systematic
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### Dictionary used

Dictionary name	20.1
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Dictionary version	20.1
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### Reporting groups

Reporting group title	Ataluren
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Reporting group description:

Ataluren was provided as a vanilla-flavored powder to be mixed with water, milk, fruit juice (except apple juice) fruit punch, or in semi-solid food (for example, yogurt, pudding, or applesauce). The dose level for ataluren was 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening. Administration within 30 minutes after a meal was recommended. Study drug dosing was based on milligrams of drug per kilogram of body weight. Because of potential changes in participant body weight over time, weight-based dose adjustment occurred every 24 weeks as required. Study drug was taken for up to 240 weeks.

Serious adverse events	Ataluren		
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 94 (32.98%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	15 / 94 (15.96%)		
occurrences causally related to treatment / all	0 / 15		
deaths causally related to treatment / all	0 / 0		
Tibia fracture			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Back injury			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fall			

subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal fracture			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Ventricular arrhythmia			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Cardiac failure			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiogenic shock			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Myocardial infarction			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Tachycardia			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Intracranial pressure increased			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			



Rectal haemorrhage			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Actinomycosis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Postoperative abscess			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	Ataluren		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	88 / 94 (93.62%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	2		
Varicose ulceration			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	2		
Surgical and medical procedures			
Tenotomy			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Haemorrhoid operation			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Nail operation			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Spinal operation			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Tooth extraction			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Wedge resection toenail			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
General disorders and administration			

site conditions			
Disease progression			
subjects affected / exposed	27 / 94 (28.72%)		
occurrences (all)	27		
Pyrexia			
subjects affected / exposed	19 / 94 (20.21%)		
occurrences (all)	24		
Asthenia			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	4		
Influenza like illness			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	6		
Malaise			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	10		
Fatigue			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	5		
Chest pain			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Infusion site pain			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Non-cardiac chest pain			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	21		
Reproductive system and breast disorders			

Testicular appendage torsion subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	16 / 94 (17.02%) 26		
Oropharyngeal pain subjects affected / exposed occurrences (all)	14 / 94 (14.89%) 24		
Epistaxis subjects affected / exposed occurrences (all)	5 / 94 (5.32%) 6		
Nasal congestion subjects affected / exposed occurrences (all)	3 / 94 (3.19%) 3		
Respiratory failure subjects affected / exposed occurrences (all)	3 / 94 (3.19%) 4		
Rhinorrhoea subjects affected / exposed occurrences (all)	3 / 94 (3.19%) 3		
Sleep apnoea syndrome subjects affected / exposed occurrences (all)	2 / 94 (2.13%) 2		
Hypoventilation subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		
Lung disorder subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		
Pulmonary congestion subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		
Psychiatric disorders			

Anxiety			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Enuresis			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Sleep disorder			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Anger			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Gender dysphoria			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Obsessive-compulsive disorder			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Investigations			
Cardiac function test abnormal			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Cortisol decreased			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Weight decreased			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	4		
Weight increased			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Cystatin C increased			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Monocyte count decreased			

subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	2		
Red blood cells urine			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	5		
Blood bilirubin increased			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Blood cholesterol increased			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Blood corticotrophin decreased			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Blood magnesium increased			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Blood potassium increased			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Blood sodium decreased			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Blood testosterone decreased			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Blood urea increased			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Blood uric acid increased			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		

Blood urine present			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Body temperature increased			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Electrocardiogram ST segment elevation			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Forced vital capacity decreased			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
High density lipoprotein increased			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Lymph node palpable			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Oxygen saturation decreased			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Urinary lipids present			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Protein urine present			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	21 / 94 (22.34%)		
occurrences (all)	66		
Femur fracture			

subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Lower limb fracture			
subjects affected / exposed	7 / 94 (7.45%)		
occurrences (all)	9		
Joint injury			
subjects affected / exposed	5 / 94 (5.32%)		
occurrences (all)	5		
Ligament sprain			
subjects affected / exposed	5 / 94 (5.32%)		
occurrences (all)	5		
Foot fracture			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	4		
Limb injury			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Lumbar vertebral fracture			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Contusion			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	3		
Humerus fracture			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Muscle strain			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Post-traumatic pain			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Tibia fracture			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Administration related reaction			



subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Arthropod bite			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Back injury			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Bone fissure			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Chest injury			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Chillblains			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Eschar			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Hand fracture			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Head injury			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Injury			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Muscle rupture			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Skin abrasion			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Spinal column injury			

subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Spinal cord injury sacral			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Spinal fracture			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Upper limb fracture			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Cardiac disorders			
Cardiomyopathy			
subjects affected / exposed	8 / 94 (8.51%)		
occurrences (all)	9		
Left ventricular dysfunction			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Cardiovascular insufficiency			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Extrasystoles			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Left ventricular hypertrophy			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Sinus tachycardia			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Nervous system disorders			
Headache			

subjects affected / exposed	29 / 94 (30.85%)		
occurrences (all)	192		
Dizziness			
subjects affected / exposed	6 / 94 (6.38%)		
occurrences (all)	6		
Migraine			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	14		
Aphonia			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Hypokinesia			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Presyncope			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Ear pain			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	4		
Motion sickness			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Eye disorders			
Cataract			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	4		
Eye allergy			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Myopia			

subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	28 / 94 (29.79%)		
occurrences (all)	69		
Abdominal pain upper			
subjects affected / exposed	14 / 94 (14.89%)		
occurrences (all)	42		
Diarrhoea			
subjects affected / exposed	13 / 94 (13.83%)		
occurrences (all)	32		
Constipation			
subjects affected / exposed	9 / 94 (9.57%)		
occurrences (all)	10		
Nausea			
subjects affected / exposed	7 / 94 (7.45%)		
occurrences (all)	28		
Abdominal pain			
subjects affected / exposed	6 / 94 (6.38%)		
occurrences (all)	11		
Abdominal discomfort			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	4		
Flatulence			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Dyspepsia			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Haemorrhoids			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Mouth ulceration			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	4		

<p>Toothache</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 94 (2.13%)</p> <p>2</p>		
<p>Anal fistula</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 94 (1.06%)</p> <p>1</p>		
<p>Eructation</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 94 (1.06%)</p> <p>1</p>		
<p>Faeces soft</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 94 (1.06%)</p> <p>1</p>		
<p>Frequent bowel movements</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 94 (1.06%)</p> <p>1</p>		
<p>Irritable bowel syndrome</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 94 (1.06%)</p> <p>1</p>		
<p>Lip swelling</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 94 (1.06%)</p> <p>3</p>		
<p>Odynophagia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 94 (1.06%)</p> <p>1</p>		
<p>Rectal haemorrhage</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 94 (1.06%)</p> <p>1</p>		
<p>Skin and subcutaneous tissue disorders</p> <p>Rash</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>8 / 94 (8.51%)</p> <p>8</p>		
<p>Eczema</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 94 (3.19%)</p> <p>4</p>		
<p>Ingrowing nail</p>			

subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Skin irritation			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Urticaria			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Dermatitis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Hyperhidrosis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Intertrigo			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Pain of skin			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Pigmentation disorder			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Pityriasis rosea			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Skin fissures			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Swelling face			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		

Dysuria			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Urine abnormality			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Incontinence			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	2		
Myoglobinuria			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Pollakiuria			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Strangury			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Endocrine disorders			
Delayed puberty			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	21 / 94 (22.34%)		
occurrences (all)	33		
Arthralgia			
subjects affected / exposed	9 / 94 (9.57%)		
occurrences (all)	13		
Scoliosis			
subjects affected / exposed	9 / 94 (9.57%)		
occurrences (all)	10		
Muscular weakness			
subjects affected / exposed	7 / 94 (7.45%)		
occurrences (all)	7		
Pain in extremity			

subjects affected / exposed	7 / 94 (7.45%)		
occurrences (all)	8		
Extremity contracture			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Musculoskeletal pain			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	7		
Neck pain			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Fracture pain			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Muscle contracture			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Spinal deformity			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Arthropathy			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Coccydynia			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Intervertebral disc compression			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Joint ankylosis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Joint contracture			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Kyphosis			



subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Limb discomfort			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Lordosis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Mastication disorder			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Musculoskeletal discomfort			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Neck mass			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Osteopenia			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Osteoporosis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Tendon disorder			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	2		
Tendonitis			

subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Torticollis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	40 / 94 (42.55%)		
occurrences (all)	88		
Gastroenteritis			
subjects affected / exposed	19 / 94 (20.21%)		
occurrences (all)	26		
Upper respiratory tract infection			
subjects affected / exposed	19 / 94 (20.21%)		
occurrences (all)	36		
Influenza			
subjects affected / exposed	9 / 94 (9.57%)		
occurrences (all)	10		
Rhinitis			
subjects affected / exposed	9 / 94 (9.57%)		
occurrences (all)	15		
Lower respiratory tract infection			
subjects affected / exposed	8 / 94 (8.51%)		
occurrences (all)	9		
Ear infection			
subjects affected / exposed	7 / 94 (7.45%)		
occurrences (all)	9		
Respiratory tract infection			
subjects affected / exposed	5 / 94 (5.32%)		
occurrences (all)	7		
Urinary tract infection			
subjects affected / exposed	5 / 94 (5.32%)		
occurrences (all)	6		
Pharyngitis			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	4		

Fungal infection			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	3		
Fungal skin infection			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Onychomycosis			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Paronychia			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Viral infection			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	3		
Actinomycosis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	2		
Body tinea			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	2		
Bronchitis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Cellulitis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Gastroenteritis viral			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Gastrointestinal infection			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		

Gastrointestinal viral infection			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	2		
Herpes zoster			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Labyrinthitis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Laryngitis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Localised infection			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Pertussis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Pharyngitis streptococcal			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Scarlet fever			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Sebaceous gland infection			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Subcutaneous abscess			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Tinea pedis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		

Tooth infection subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		
Viral pharyngitis subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	5 / 94 (5.32%) 5		
Dehydration subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		
Hypercholesterolaemia subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		
Hypokalaemia subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		
Obesity subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		
Overweight subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		
Vitamin D deficiency subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 February 2013	<p>In addition to minor administrative updates and editing to fix typographical and grammatical errors, the following changes were made to the protocol:</p> <ul style="list-style-type: none"><li>• The ataluren treatment period was extended from 48 to 96 weeks and related text modified for the schedule of events, frequency of site visits and periodic assessments throughout the protocol to be consistent with the extension of treatment.</li><li>• Text was added regarding the addition of a Data Monitoring Committee.</li></ul>
20 February 2014	<p>In addition to administrative changes, formatting edits, and inclusion of additional information from other ataluren studies, or deletion of general information text, the following updates were made:</p> <ul style="list-style-type: none"><li>• The ataluren treatment period was extended from 96 to 144 weeks and related text modified for the schedule of events, frequency of site visits, and periodic assessments throughout the protocol to be consistent with the extension of treatment.</li><li>• A new section on Potential Drug Interactions was added, and the Prior and Concomitant Therapies section was updated to include a caution about concomitant use of ataluren and drugs that metabolized by cytochrome P450 (CYP)2C8 or CYP2C9, coumarin, phenytoin, drugs that are inducers of UDP glucuronosyltransferase family 1 member A9 (UGT1A9), and drugs that are substrates of UGT1A9, organic anion transporter 1 (OAT1), organic anion transporter 1 (OAT3), or Organic anion transporting polypeptide 1B3 (OATP1B3).</li><li>• To harmonize this protocol with others in the clinical development program, text regarding the withdrawal of participants due to the participant's condition substantially worsening after initiating study drug was modified to include the worsening of cardiac events such as QTc interval limits, new evidence of symptomatic cardiomyopathy, and significant decrease in left ventricular ejection fraction.</li><li>• A new section, Lipid Profile, was added to provide for evaluation of total cholesterol, low density lipoprotein, high density lipoprotein, and triglycerides at each visit to monitor for changes in lipid profile values.</li><li>• A new section, Blood Pressure Assessment, was added to provide for blood pressure monitoring via standardized procedures at each visit.</li><li>• Study Drug Accountability section was modified to specify that ataluren was to be stored under temperature-monitored conditions, and Study Drug Preparation and Storage was modified to specify that the study drug sachets should be monitored during storage at room temperature.</li></ul>
12 January 2015	<p>In addition to minor administrative updates and the inclusion of additional information pertaining to other ataluren studies, this amendment made the following changes to the protocol:</p> <ul style="list-style-type: none"><li>• The ataluren treatment period was extended from 144 to 192 weeks and related text modified for the schedule of events, frequency of site visits, and periodic assessments throughout the protocol to be consistent with the extension of treatment.</li><li>• The language was modified to clarify that weight-based dose adjustment was to occur every 6 months.</li><li>• The post-treatment visit language was updated to specify that for participants discontinuing the study in order to transition to commercially available ataluren, an End-of-Treatment (EOT) visit should be performed for that participant. However, a 6-week post-treatment visit was not required for these participants.</li><li>• The language under Study Drug Administration clarified that participants were required to be at the site for the 24-week (6-month) re-weigh visit.</li></ul>

18 November 2015	<p>In addition to administrative changes and updates to other ataluren studies, this protocol was updated to include the following study-related changes:</p> <ul style="list-style-type: none"> <li>• The ataluren treatment period was extended from 192 to 240 weeks and related text modified for the schedule of events, frequency of site visits, and periodic assessments throughout the protocol to be consistent with the extension of treatment.</li> <li>• Updated the language regarding the conversion of ambulatory participants to commercial drug to specify that if the participant terminated the study early because ataluren was commercially available in that country, then the participant only needed to return for the EOT Visit.</li> <li>• Language was updated to change the reporting of pregnancy of female partners, unresolved AEs, and investigator site reporting requirements for AEs from Mapi Safety to the PTC Therapeutics Safety department.</li> <li>• If the participant discontinued prematurely, except participants switching to commercial ataluren, (that is, before 240) and the last visit to the Investigator site occurred &gt;3 weeks previously, the procedures that would normally be performed at Week 240 should be performed as a Premature Discontinuation Visit before the participant leaves the study.</li> </ul>
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Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported