



Clinical trial results:

A Phase 3 Extension Study of Ataluren (PTC124) in Patients With Nonsense Mutation Dystrophinopathy

Summary

| | |
|--------------------------|----------------------------|
| EudraCT number | 2013-005489-20 |
| Trial protocol | SE GB BE DE IT ES CZ FR BG |
| Global end of trial date | 12 June 2018 |

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-020e-DMD |
|-----------------------|--------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02090959 |
| 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 | PTC Trial Disclosure, PTC Therapeutics, Inc., +353 19068700, ptctrtrialdisclosure@ptcbio.com |
| Scientific contact | PTC Trial Disclosure, PTC Therapeutics, Inc., +353 19068700, ptctrtrialdisclosure@ptcbio.com |

Notes:

Paediatric regulatory details

| | |
|--|-----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 12 June 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 12 June 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 12 June 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The purpose of this extension study was to obtain long-term safety data of ataluren administered 3 times a day at 10, 10, and 20 milligrams/kilogram (mg/kg) to augment the ataluren safety database.

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 | 20 March 2014 |
| 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: 10 |
| Country: Number of subjects enrolled | Belgium: 6 |
| Country: Number of subjects enrolled | Brazil: 5 |
| Country: Number of subjects enrolled | Bulgaria: 2 |
| Country: Number of subjects enrolled | Canada: 7 |
| Country: Number of subjects enrolled | Chile: 14 |
| Country: Number of subjects enrolled | Czech Republic: 1 |
| Country: Number of subjects enrolled | France: 14 |
| Country: Number of subjects enrolled | Germany: 10 |
| Country: Number of subjects enrolled | Israel: 3 |
| Country: Number of subjects enrolled | Italy: 11 |
| Country: Number of subjects enrolled | Poland: 8 |
| Country: Number of subjects enrolled | Korea, Republic of: 4 |
| Country: Number of subjects enrolled | Spain: 22 |
| Country: Number of subjects enrolled | Sweden: 7 |
| Country: Number of subjects enrolled | Switzerland: 3 |
| Country: Number of subjects enrolled | Turkey: 14 |
| Country: Number of subjects enrolled | United Kingdom: 14 |
| Country: Number of subjects enrolled | United States: 63 |

| | |
|------------------------------------|-----|
| Worldwide total number of subjects | 218 |
| EEA total number of subjects | 95 |

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) | 175 |
| Adolescents (12-17 years) | 43 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

All participants who successfully completed the double-blind, placebo-controlled Phase 3 study (PTC124-GD-020-DMD [NCT01826487]) were screened for this open-label extension study.

Pre-assignment

Screening details:

A total of 221 participants completed the double-blind Phase 3 Study PTC124-GD-020-DMD. Of the 221 participants who completed Study PTC124-GD-020-DMD, 219 participants were enrolled in this open-label extension study and 218 were treated.

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 |
|-----------|----------|

Arm description:

Participants received ataluren suspension orally 3 times a day (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 up to 144 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 per the dose and schedule specified in the arm.

| Number of subjects in period 1 | Ataluren |
|---|----------|
| Started | 218 |
| Completed | 68 |
| Not completed | 150 |
| Switched to commercial supply | 88 |
| Consent withdrawn by subject | 10 |
| Move to medical need program | 3 |
| Adverse event, non-fatal | 1 |
| Study termination | 6 |
| Investigator decision | 2 |
| Transfer for compassionate use medicine | 4 |
| Other than specified | 2 |

| | |
|---------------------------|----|
| Entered in to other study | 34 |
|---------------------------|----|

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------|
| Reporting group title | Ataluren |
|-----------------------|----------|

Reporting group description:

Participants received ataluren suspension orally 3 times a day (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 up to 144 weeks.

| Reporting group values | Ataluren | Total | |
|---|------------|-------|--|
| Number of subjects | 218 | 218 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Children (2-11 years) | 175 | 175 | |
| Adolescents (12-17 years) | 43 | 43 | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 9.9 | | |
| standard deviation | ± 1.78 | - | |
| Sex: Female, Male | | | |
| Units: Subjects | | | |
| Female | 0 | 0 | |
| Male | 218 | 218 | |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| White | 169 | 169 | |
| Black | 2 | 2 | |
| Asian | 13 | 13 | |
| Hispanic | 12 | 12 | |
| Other | 8 | 8 | |
| Missing | 14 | 14 | |
| 6 Minute Walk Distance (6MWD) | | | |
| The 6MWD test was performed in a 30 meters long flat corridor, where the participant was instructed to walk as far as possible, back and forth around two cones, with the permission to slow down, rest, or stop if needed. Ambulation was assessed via the 6MWD test following standardized procedures by measuring the 6MWD in meters. Participants were not permitted to use assistive devices (walker, long leg braces, or short leg braces) during the 6MWD test. Number of participants analyzed for this baseline measure are 198 (ambulatory participants). | | | |
| Units: meters | | | |
| arithmetic mean | 349.885 | | |
| standard deviation | ± 105.7913 | - | |
| Time to Stand From Supine Position | | | |
| Number of participants analyzed for this baseline measure are 199. | | | |
| Units: seconds | | | |
| arithmetic mean | 13.0 | | |
| standard deviation | ± 10.34 | - | |
| Time to Walk/Run 10 Meters | | | |
| Number of participants analyzed for this baseline measure are 215. | | | |
| Units: seconds | | | |
| arithmetic mean | 9.31 | | |
| standard deviation | ± 7.388 | - | |

| | | | |
|---|----------|---|--|
| Time to Climb 4 Stairs | | | |
| Number of participants analyzed for this baseline measure are 203. | | | |
| Units: seconds | | | |
| arithmetic mean | 9.03 | | |
| standard deviation | ± 8.939 | - | |
| Time to Descend 4 Stairs | | | |
| Number of participants analyzed for this baseline measure are 204. | | | |
| Units: seconds | | | |
| arithmetic mean | 7.52 | | |
| standard deviation | ± 8.401 | - | |
| North Star Ambulatory Assessment (NSAA) Total Score | | | |
| NSAA:tests of 17 abilities: ability to stand, rise from floor, get from lying to sitting, 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 without any assistance." Sum of these 17 scores was reported as ordinal total score, which can be transformed to a linear total score from 0(worst) to 100(best). Number of participants analyzed=195 (ambulatory participants with a baseline value). | | | |
| Units: units on a scale | | | |
| arithmetic mean | 20.73 | | |
| standard deviation | ± 8.513 | - | |
| Performance Upper Limb (PUL) Total Score | | | |
| PUL scale includes 22 items; an entry item defining the starting functional level, and 21 items subdivided into shoulder level (4 items), elbow level (9 items), and distal level (8 items) dimensions. Scoring options per item may vary from 0-1 and 0-6, with higher values corresponding to better performance. Each dimension was scored separately with a maximum score of 16 for shoulder level, 34 for elbow level, and 24 for distal level. Total score was calculated by adding the 3 level scores (maximum global score of 74). Number of participants analyzed for this baseline measure are 210. | | | |
| Units: units on a scale | | | |
| arithmetic mean | 68.7 | | |
| standard deviation | ± 4.61 | - | |
| Percent Predicted Forced Vital Capacity (FVC) | | | |
| FVC is a standard pulmonary function test. FVC was defined as the volume of air that can forcibly be blown out after full inspiration in the upright position, measured in liters. Percent predicted FVC (in %) = [(observed FVC)/(predicted FVC)]*100. Number of participants analyzed for this baseline measure are 210. | | | |
| Units: percent predicted FVC | | | |
| arithmetic mean | 59.42 | | |
| standard deviation | ± 13.843 | - | |
| Percent Predicted Forced Expiratory Volume in 1 Second (FEV1) | | | |
| FEV1 is a standard pulmonary function test. FEV1 was defined as the volume of air that can forcibly be blown out in 1 second, after full inspiration in the upright position, measured in liters. Percent predicted FEV1 (in %) = [(observed FEV1)/(predicted FEV1)]*100. Number of participants analyzed for this baseline measure are 209. | | | |
| Units: percent predicted FEV1 | | | |
| arithmetic mean | 53.76 | | |
| standard deviation | ± 12.870 | - | |
| Peak Expiratory Flow (PEF) | | | |
| PEF was defined as the maximum airflow during a forced expiration beginning with the lungs fully inflated. Number of participants analyzed for this baseline measure are 213. | | | |
| Units: liters/second (L/sec) | | | |
| arithmetic mean | 3.36 | | |
| standard deviation | ± 1.055 | - | |
| Peak Cough Flow (PCF) | | | |
| PCF measures an individual's maximum speed of expiration during cough. Number of participants | | | |

| | | | |
|---|---------|---|--|
| analyzed for this baseline measure are 194. | | | |
| Units: L/sec | | | |
| arithmetic mean | 3.30 | | |
| standard deviation | ± 1.139 | - | |
| 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. Following PODCI domains were prespecified in protocol for analysis: 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 for this baseline measure are 216. | | | |
| Units: units on a scale | | | |
| arithmetic mean | 74.6 | | |
| standard deviation | ± 23.66 | - | |
| Systolic blood pressure | | | |
| Number of participants analyzed for this baseline measure are 217. | | | |
| Units: millimeters of mercury (mm Hg) | | | |
| arithmetic mean | 106.3 | | |
| standard deviation | ± 10.72 | - | |
| Diastolic blood pressure | | | |
| Number of participants analyzed for this baseline measure are 217. | | | |
| Units: mm Hg | | | |
| arithmetic mean | 68.6 | | |
| standard deviation | ± 11.01 | - | |
| Pulse Rate | | | |
| Number of participants analyzed for this baseline measure are 217. | | | |
| Units: beats/minute | | | |
| arithmetic mean | 97.0 | | |
| standard deviation | ± 13.31 | - | |
| Body Temperature | | | |
| Number of participants analyzed for this baseline measure are 217. | | | |
| Units: degrees centigrade | | | |
| arithmetic mean | 36.47 | | |
| standard deviation | ± 0.453 | - | |

End points

End points reporting groups

| | |
|---|----------|
| Reporting group title | Ataluren |
| Reporting group description: | |
| Participants received ataluren suspension orally 3 times a day (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 up to 144 weeks. | |

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

| | |
|---|--|
| End point title | Number of Participants With Treatment-Emergent Adverse Events (TEAEs) ^[1] |
| End point description: | |
| An adverse event (AE): any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. Severity of AEs: graded per Common Terminology Criteria for AEs (CTCAE), Version 3.0 as Grade 1 (mild), 2 (moderate), 3 (severe), 4 (life-threatening), 5 (death). Drug-related AEs: AEs with possible, probable, unlikely relationship, or unrelated to study drug. Serious AEs (SAEs): death, a life-threatening AE, inpatient hospitalization or prolongation of hospitalization, persistent or significant disability or incapacity, a congenital anomaly or birth defect, or an important medical event that required medical intervention. TEAE: an AE that occurred from first dose of study drug in this study to 6 weeks after last dose. A summary of other non-serious AEs and all SAEs, regardless of causality is located in Reported AE section. As Treated (AT) population: all participants who received at least 1 dose of ataluren treatment in this study. | |
| End point type | Primary |
| End point timeframe: | |
| Baseline (Day 1) up to 6 weeks post-treatment (Week 150) | |
| 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: Endpoint is safety in nature | |

| End point values | Ataluren | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 218 | | | |
| Units: participants | | | | |
| Any AEs | 202 | | | |
| SAEs | 24 | | | |
| Drug-Related AEs | 44 | | | |
| AEs Leading to Withdrawal From Study | 1 | | | |
| Mild AEs | 87 | | | |
| Moderate AEs | 71 | | | |
| Severe AEs | 42 | | | |
| Life-threatening AEs | 2 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Abnormalities in Clinical Laboratory

Parameters

| | |
|-----------------|--|
| End point title | Number of Participants With Abnormalities in Clinical Laboratory Parameters ^[2] |
|-----------------|--|

End point description:

Abnormalities in laboratory variables as pre-defined in protocol for safety-monitoring were: Hepatic (Serum alanine aminotransferase [ALT]: increase of greater than [$>$] 150 units/liter [U/L] with stable or decrease of creatinine kinase [CK]; Serum glutamyl amino transferase [GGT] [U/L]: Grade 2 [$>2.5 - 5.0$ * upper limit of normal {ULN}], renal (Serum cystatin C milligrams/liter [mg/L] $>1.33 - 2.00$ mg/L; Serum blood urea nitrogen [UREAN] [millimoles/liter {mmol/L}] greater than or equal to [\geq] $1.5 - 3.0$ * ULN; Urine occult blood: 2+ [Small], 3+ [Moderate], 4+ [Large]), and electrolytes (Serum sodium: low [mmol/L], Grade 3-4 [less than [$<$] 130 mmol/L]; serum potassium: high [mmol/L], Grade 3-4 [>6.0 mmol/L]; and Serum bicarbonate [mmol/L]: Grade 2 [$<16 - 11$ mmol/L]). AT population included all participants who received at least 1 dose of ataluren treatment in this extension study.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline (Day 1) up to 6 weeks post-treatment (Week 150)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Endpoint is safety in nature

| | | | | |
|-----------------------------|-----------------|--|--|--|
| End point values | Ataluren | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 218 | | | |
| Units: participants | 29 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 6MWD at Week 144

| | |
|-----------------|--|
| End point title | Change From Baseline in 6MWD at Week 144 |
|-----------------|--|

End point description:

The 6MWD test was performed in a 30 meters long flat corridor, where the participant was instructed to walk as far as possible, back and forth around two cones, with the permission to slow down, rest, or stop if needed. Ambulation was assessed via the 6MWD test following standardized procedures by measuring the 6MWD in meters. Participants were not permitted to use assistive devices (walker, long leg braces, or short leg braces) during the 6MWD test. AT population included all participants who received at least 1 dose of ataluren treatment in this extension study. Here, 'Overall number of participants analyzed' = participants who had both baseline and post-baseline 6MWD value at specified timepoint.

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|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 144

| End point values | Ataluren | | | |
|--------------------------------------|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 26 | | | |
| Units: meters | | | | |
| arithmetic mean (standard deviation) | -98.18 (\pm 86.604) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Time to Stand From Supine Position at Week 144

| | |
|-----------------|--|
| End point title | Change From Baseline in Time to Stand From Supine Position at Week 144 |
|-----------------|--|

End point description:

If the time taken to perform this test exceeded 30 seconds or if a participant could not perform this test due to disease progression, a value of 30 seconds was used. AT population included all participants who received at least 1 dose of ataluren treatment in this extension study. Here, 'Overall number of participants analyzed' = participants who had both baseline and post-baseline value of this parameter at specified timepoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 144

| End point values | Ataluren | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | 5.22 (\pm 5.104) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Time to Walk/Run 10 Meters at Week 144

| | |
|-----------------|--|
| End point title | Change From Baseline in Time to Walk/Run 10 Meters at Week 144 |
|-----------------|--|

End point description:

If the time taken to perform this test exceeded 30 seconds or if a participant could not perform this test due to disease progression, a value of 30 seconds was used. AT population included all participants who received at least 1 dose of ataluren treatment in this extension study. Here, 'Overall number of participants analyzed' = participants who had both baseline and post-baseline value of this parameter at specified timepoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 144

| | | | | |
|--------------------------------------|---------------------|--|--|--|
| End point values | Ataluren | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 27 | | | |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | 2.29 (\pm 1.991) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Time to Climb 4 Stairs at Week 144

| | |
|-----------------|--|
| End point title | Change From Baseline in Time to Climb 4 Stairs at Week 144 |
|-----------------|--|

End point description:

If the time taken to perform this test exceeded 30 seconds or if a participant could not perform this test due to disease progression, a value of 30 seconds was used. AT population included all participants who received at least 1 dose of ataluren treatment in this extension study. Here, 'Overall number of participants analyzed' = participants who had both baseline and post-baseline value of this parameter at specified timepoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 144

| | | | | |
|--------------------------------------|---------------------|--|--|--|
| End point values | Ataluren | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 22 | | | |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | 4.01 (\pm 7.260) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Time to Descend 4 Stairs at Week 144

| | |
|-----------------|--|
| End point title | Change From Baseline in Time to Descend 4 Stairs at Week 144 |
|-----------------|--|

End point description:

If the time taken to perform this test exceeded 30 seconds or if a participant could not perform this test due to disease progression, a value of 30 seconds was used. AT population included all participants who received at least 1 dose of ataluren treatment in this extension study. Here, 'Overall number of participants analyzed' = participants who had both baseline and post-baseline value of this parameter at

specified timepoint.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 144 | |

| | | | | |
|--------------------------------------|---------------------|--|--|--|
| End point values | Ataluren | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 22 | | | |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | 2.45 (\pm 5.853) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Physical Function Total Score as Measured by NSAA at Week 144

| | |
|-----------------|---|
| End point title | Change From Baseline in Physical Function Total Score as Measured by NSAA at Week 144 |
|-----------------|---|

End point description:

NSAA comprised tests for 17 abilities of a participant, such as 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 without any assistance." Sum of these scores (except for 'raise one's head' activity score) was reported as the 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. AT population included all participants who received at least 1 dose of ataluren treatment in this extension study. Here, 'Overall number of participants analyzed' = participants who had both baseline and post-baseline value of this parameter at specified timepoint.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 144 | |

| | | | | |
|--------------------------------------|----------------------|--|--|--|
| End point values | Ataluren | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | -7.95 (\pm 5.611) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in PUL Total Score at Week 144

| | |
|-----------------|---|
| End point title | Change From Baseline in PUL Total Score at Week 144 |
|-----------------|---|

End point description:

The PUL was used to assess motor performance of the upper limb. The PUL scale includes 22 items; an entry item defining the starting functional level, and 21 items subdivided into shoulder level (4 items), elbow level (9 items), and distal level (8 items) dimensions. Scoring options per item may not be uniform and may vary from 0-1 and 0-6, according to the performance, with higher values corresponding to better performance. Each dimension was scored separately with a maximum score of 16 for shoulder level, 34 for elbow level, and 24 for distal level. Total score was calculated by adding the 3 level scores (maximum global score of 74). AT population included all participants who received at least 1 dose of ataluren treatment in this extension study. Here, 'Overall number of participants analyzed' = participants who had both baseline and post-baseline value of this parameter at specified timepoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 144

| End point values | Ataluren | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 44 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | -4.0 (± 7.49) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Percent Predicted FVC as Measured by Spirometry at Week 144

| | |
|-----------------|---|
| End point title | Change From Baseline in Percent Predicted FVC as Measured by Spirometry at Week 144 |
|-----------------|---|

End point description:

FVC is a standard pulmonary function test. FVC was defined as the volume of air that can forcibly be blown out after full inspiration in the upright position, measured in liters. Percent predicted FVC (in %) = [(observed FVC)/(predicted FVC)]*100. AT population included all participants who received at least 1 dose of ataluren treatment in this extension study. Here, 'Overall number of participants analyzed' = participants who had both baseline and post-baseline value of this parameter at specified timepoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 144

| End point values | Ataluren | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 63 | | | |
| Units: percent predicted FVC | | | | |
| arithmetic mean (standard deviation) | 3.51 (\pm 14.253) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Percent Predicted FEV1 as Measured by Spirometry at Week 144

| | |
|-----------------|--|
| End point title | Change From Baseline in Percent Predicted FEV1 as Measured by Spirometry at Week 144 |
|-----------------|--|

End point description:

FEV1 is a standard pulmonary function test. FEV1 was defined as the volume of air that can forcibly be blown out in 1 second, after full inspiration in the upright position, measured in liters. Percent predicted FEV1 (in %) = [(observed FEV1)/(predicted FEV1)]*100. AT population included all participants who received at least 1 dose of ataluren treatment in this extension study. Here, 'Overall number of participants analyzed' = participants who had both baseline and post-baseline value of this parameter at specified timepoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 144

| End point values | Ataluren | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 63 | | | |
| Units: percent predicted FEV1 | | | | |
| arithmetic mean (standard deviation) | 1.40 (\pm 15.319) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in PEF as Measured by Spirometry at Week 144

| | |
|-----------------|---|
| End point title | Change From Baseline in PEF as Measured by Spirometry at Week 144 |
|-----------------|---|

End point description:

PEF was defined as the maximum airflow during a forced expiration beginning with the lungs fully inflated. AT population included all participants who received at least 1 dose of ataluren treatment in this extension study. Here, 'Overall number of participants analyzed' = participants who had both baseline and post-baseline value of this parameter at specified timepoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 144

| | | | | |
|--------------------------------------|---------------------|--|--|--|
| End point values | Ataluren | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 65 | | | |
| Units: L/sec | | | | |
| arithmetic mean (standard deviation) | 0.23 (\pm 1.099) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in PCF as Measured by Spirometry at Week 144

| | |
|-----------------|---|
| End point title | Change From Baseline in PCF as Measured by Spirometry at Week 144 |
|-----------------|---|

End point description:

PCF measures an individual's maximum speed of expiration during cough. AT population included all participants who received at least 1 dose of ataluren treatment in this extension study. Here, 'Overall number of participants analyzed' = participants who had both baseline and post-baseline value of this parameter at specified timepoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 144

| | | | | |
|--------------------------------------|---------------------|--|--|--|
| End point values | Ataluren | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 57 | | | |
| Units: L/sec | | | | |
| arithmetic mean (standard deviation) | 0.53 (\pm 1.281) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in PODCI Transfers/Basic Mobility Score at Week 144

| | |
|-----------------|--|
| End point title | Change From Baseline in PODCI Transfers/Basic Mobility Score at Week 144 |
|-----------------|--|

End point description:

Changes in health-related quality of life (HRQL) were measured via the PODCI questionnaire that has been shown to correlate with disease progression and clinical outcome measures in DMD. 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. The following PODCI domain was prespecified in the protocol for analysis: Transfers/Basic Mobility domain assesses difficulty experienced in performing routine motor activities in daily life. Each domain was scored from 0 to 100, with 0 representing a poor outcome/worse health, while 100 representing the highest level of functioning and least pain. AT population included all participants who received at least 1 dose of ataluren treatment in this extension study. Here, 'Overall number of participants analyzed' = participants who had both baseline and post-baseline value of this parameter at specified timepoint.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 144 | |

| End point values | Ataluren | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 65 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | -29.3 (± 25.05) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Change From Baseline in Activities of Daily Living and Disease Status at Week 144, 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 144, as Assessed by a Standardized Survey Administered by Site Personnel |
|-----------------|--|

End point description:

Changes in activities of daily living and disease symptoms were captured via a DMD-specific survey administered by Site personnel. At screening/baseline, participant and/or parent/caregiver were asked to identify any activities of daily living or symptoms that were affected by participant's DMD. At post-baseline visit (Week 144), the same participant and/or parent/caregiver was asked to describe any changes from baseline in those activities of daily living/symptoms, within the following categories: physical functioning (PF); general energy level (GEL); cognition/school function (C/SF); emotional/social functioning (E/SF); and sleep. Changes from baseline were reported on a 5-point Likert scale: 1 (much better), 2 (slightly better), 3 (unchanged), 4 (slightly worse), or 5 (much worse). AT population included all participants who received at least 1 dose of ataluren treatment in this extension study. Here, 'n' signifies participants evaluable for specified categories.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 144 | |

| End point values | Ataluren | | | |
|--|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 218 | | | |
| Units: participants | | | | |
| PF- Walking: Much better (n=143) | 6 | | | |
| PF- Walking: Slightly better (n=143) | 3 | | | |
| PF- Walking: Unchanged (n=143) | 47 | | | |
| PF- Walking: Slightly worse (n=143) | 32 | | | |
| PF- Walking: Much worse (n=143) | 55 | | | |
| PF- Climbing stairs: Much better (n=141) | 6 | | | |
| PF- Climbing stairs: Slightly better (n=141) | 4 | | | |
| PF- Climbing stairs: Unchanged (n=141) | 37 | | | |
| PF- Climbing stairs: Slightly worse (n=141) | 29 | | | |
| PF- Climbing stairs: Much worse (n=141) | 65 | | | |
| PF- Upper Extremity Activity: Much better (n=119) | 5 | | | |
| PF-Upper Extremity Activity:Slightly better(n=119) | 6 | | | |
| PF- Upper Extremity Activity: Unchanged (n=119) | 75 | | | |
| PF- Upper Extremity Activity:Slightly worse(n=119) | 21 | | | |
| PF- Upper Extremity Activity: Much worse (n=119) | 12 | | | |
| PF- Other: Much better (n=62) | 3 | | | |
| PF- Other: Slightly better (n=62) | 2 | | | |
| PF- Other: Unchanged (n=62) | 29 | | | |
| PF- Other: Slightly worse (n=62) | 13 | | | |
| PF- Other: Much worse (n=62) | 15 | | | |
| E/SF: Much better (n=134) | 13 | | | |
| E/SF: Slightly better (n=134) | 16 | | | |
| E/SF: Unchanged (n=134) | 93 | | | |
| E/SF: Slightly worse (n=134) | 7 | | | |
| E/SF: Much worse (n=134) | 5 | | | |
| C/SF: Much better (n=133) | 9 | | | |
| C/SF: Slightly better (n=133) | 24 | | | |
| C/SF: Unchanged (n=133) | 92 | | | |
| C/SF: Sightly worse (n=133) | 8 | | | |
| C/SF: Much worse (n=133) | 0 | | | |
| GEL: Much better (n=127) | 8 | | | |
| GEL: Slightly better (n=127) | 8 | | | |
| GEL: Unchanged (n=127) | 82 | | | |
| GEL: Slightly worse (n=127) | 21 | | | |
| GEL: Much worse (n=127) | 8 | | | |
| Sleep: Much better (n=128) | 11 | | | |
| Sleep: Slightly better (n=128) | 11 | | | |
| Sleep: Unchanged (n=128) | 95 | | | |
| Sleep: Slightly worse (n=128) | 9 | | | |
| Sleep: Much worse (n=128) | 2 | | | |
| Other: Much better (n=31) | 2 | | | |

| | | | | |
|-------------------------------|----|--|--|--|
| Other: Slightly better (n=31) | 2 | | | |
| Other: Unchanged (n=31) | 12 | | | |
| Other: Slightly worse (n=31) | 8 | | | |
| Other: Much worse (n=31) | 7 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Ataluren Plasma Concentration

| | |
|-----------------|-------------------------------|
| End point title | Ataluren Plasma Concentration |
|-----------------|-------------------------------|

End point description:

Pre-dose ataluren plasma concentrations prior to morning ataluren administration at each clinic visit was assessed using a validated high performance liquid chromatography with tandem mass spectrometry (HPLC/MS-MS) method. AT population included all participants who received at least 1 dose of ataluren treatment in this extension study. Here, 'n' signifies participants evaluable for this outcome measure at specified timepoints.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Pre-dose at Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, and 144

| End point values | Ataluren | | | |
|--------------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 218 | | | |
| Units: micrograms/milliliter (µg/mL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 12 (n=210) | 4.5231 (± 5.08583) | | | |
| Week 24 (n=211) | 4.4817 (± 5.65883) | | | |
| Week 36 (n=205) | 5.1551 (± 5.67555) | | | |
| Week 48 (n=201) | 5.2221 (± 5.32846) | | | |
| Week 60 (n=191) | 5.0396 (± 5.07812) | | | |
| Week 72 (n=180) | 6.0677 (± 6.05912) | | | |
| Week 84 (n=171) | 5.4673 (± 5.15083) | | | |
| Week 96 (n=160) | 5.8870 (± 5.90954) | | | |
| Week 108 (n=133) | 5.5905 (± 6.48016) | | | |
| Week 120 (n=119) | 5.2406 (± 5.69648) | | | |
| Week 132 (n=94) | 6.6729 (± 7.03882) | | | |
| Week 144 (n=66) | 5.3898 (± 6.28487) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Systolic and Diastolic Blood Pressure at Week 144

| | |
|-----------------|---|
| End point title | Change From Baseline in Systolic and Diastolic Blood Pressure at Week 144 |
|-----------------|---|

End point description:

Blood pressure determination was performed with the participant in a sitting position after a 5-minute rest. AT population included all participants who received at least 1 dose of ataluren treatment in this extension study. Here, 'n' = participants who had both baseline and post-baseline value of this parameter at specified timepoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 144

| End point values | Ataluren | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 217 | | | |
| Units: mmHg | | | | |
| arithmetic mean (standard deviation) | | | | |
| Systolic blood pressure (n=68) | 0.8 (± 11.86) | | | |
| Diastolic blood pressure (n=63) | 1.3 (± 11.60) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pulse Rate at Week 144

| | |
|-----------------|--|
| End point title | Change From Baseline in Pulse Rate at Week 144 |
|-----------------|--|

End point description:

Pulse rate determination was performed with the participant in a sitting position after a 5-minute rest. AT population included all participants who received at least 1 dose of ataluren treatment in this extension study. Here, 'Overall number of participants analyzed' = participants who had both baseline and post-baseline value of this parameter at specified timepoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 144

| | | | | |
|--------------------------------------|---------------------|--|--|--|
| End point values | Ataluren | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 68 | | | |
| Units: beats/minute | | | | |
| arithmetic mean (standard deviation) | -0.9 (\pm 13.00) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Temperature at Week 144

| | |
|--|--|
| End point title | Change From Baseline in Body Temperature at Week 144 |
| End point description: | |
| AT population included all participants who received at least 1 dose of ataluren treatment in this extension study. Here, 'Overall number of participants analyzed' = participants who had both baseline and post-baseline value of this parameter at specified timepoint. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 144 | |

| | | | | |
|--------------------------------------|---------------------|--|--|--|
| End point values | Ataluren | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 68 | | | |
| Units: degrees centigrade | | | | |
| arithmetic mean (standard deviation) | 0.05 (\pm 0.545) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline (Day 1) up to 6 weeks post-treatment (Week 150)

Adverse event reporting additional description:

AT population included all participants who received at least 1 dose of ataluren treatment in this extension study.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------|
| 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 up to 144 weeks.

| Serious adverse events | Ataluren | | |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 24 / 218 (11.01%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Exposure to communicable disease | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Femur fracture | | | |
| subjects affected / exposed | 5 / 218 (2.29%) | | |
| occurrences causally related to treatment / all | 0 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hip fracture | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Laceration | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 2 / 218 (0.92%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal compression fracture | | | |
| subjects affected / exposed | 2 / 218 (0.92%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Congenital, familial and genetic disorders | | | |
| Transposition of the great vessels | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ventricular septal defect | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Bradycardia | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Colitis | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intussusception | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypoxia | | | |
| subjects affected / exposed | 2 / 218 (0.92%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Pneumonia aspiration | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary artery stenosis | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Flank pain | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Joint contracture | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tendinous contracture | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Adenoiditis | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Appendicitis | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chronic sinusitis | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Varicella | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 1 / 218 (0.46%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Ataluren | | |
|---|--------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 201 / 218 (92.20%) | | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 48 / 218 (22.02%) | | |
| occurrences (all) | 76 | | |
| Ligament sprain | | | |
| subjects affected / exposed | 19 / 218 (8.72%) | | |
| occurrences (all) | 22 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 42 / 218 (19.27%) | | |
| occurrences (all) | 116 | | |
| General disorders and administration site conditions | | | |
| Disease progression | | | |
| subjects affected / exposed | 56 / 218 (25.69%) | | |
| occurrences (all) | 56 | | |
| Pyrexia | | | |
| subjects affected / exposed | 26 / 218 (11.93%) | | |
| occurrences (all) | 33 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 18 / 218 (8.26%) | | |
| occurrences (all) | 20 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 17 / 218 (7.80%) | | |
| occurrences (all) | 22 | | |
| Nausea | | | |
| subjects affected / exposed | 16 / 218 (7.34%) | | |
| occurrences (all) | 27 | | |
| Vomiting | | | |
| subjects affected / exposed | 37 / 218 (16.97%) | | |
| occurrences (all) | 71 | | |

| | | | |
|--|---|--|--|
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 26 / 218 (11.93%) 40 | | |
| Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all) | 20 / 218 (9.17%) 26 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) | 14 / 218 (6.42%) 20 27 / 218 (12.39%) 29 26 / 218 (11.93%) 41 | | |
| Infections and infestations Ear infection subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) | 11 / 218 (5.05%) 12 18 / 218 (8.26%) 25 23 / 218 (10.55%) 30 57 / 218 (26.15%) 99 28 / 218 (12.84%) 62 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 19 November 2015 | <p>Changes to the conduct of the study included the following:</p> <ul style="list-style-type: none">• Study treatment period was extended from 96 weeks to 144 weeks.• Blood drawing requirements were updated to specify the number of tubes for blood trough PK would be 10 rather than 8 and the total blood volume drawn from screening to end of study would be 152 milliliters (mL).• Language discouraging the use of cardiac drugs for prophylactic/treatment of congestive heart failure (CHF) was removed.• Language regarding weight-based dosing assessments was simplified to specify assessments be made every 6 months.• Exempted participants who terminated from study early due to a transition to commercial ataluren from the 6-week post treatment follow-up visit.• Removed requirement for videotaping the 6MWT, timed function tests, NSAA, and PUL assessments. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated early per Sponsor decision due to commercial availability of ataluren.

Notes: