



## Clinical trial results: A Phase 2a Study of Ataluren (PTC124) in Nonambulatory Patients with Nonsense-Mutation-Mediated Duchenne/Becker Muscular Dystrophy Summary

EudraCT number	2009-013169-24
Trial protocol	GB
Global end of trial date	09 July 2010

### Results information

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

### Trial information

#### Trial identification

Sponsor protocol code	PTC124-GD-008-DMD
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01009294
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)	EMEA-000115-PIP01-09
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	23 March 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 March 2010
Global end of trial reached?	Yes
Global end of trial date	09 July 2010
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the safety and tolerability of ataluren in nonambulatory participants with Nonsense-Mutation-Mediated Duchenne/Becker Muscular Dystrophy (nmDBMD).

Protection of trial subjects:

The trial was conducted in accordance with Declaration of Helsinki (revised version of Edinburgh, Scotland, 2000), FDA GCP regulations, and the International Conference on Harmonisation (ICH) GCP guidance documents.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 January 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	6
EEA total number of subjects	0

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	3
Adults (18-64 years)	3
From 65 to 84 years	0



## Subject disposition

### Recruitment

Recruitment details:

A total of 11 participants with nmDBMD and were nonambulatory signed the informed consent form and were screened for eligibility. Six of these participants were enrolled at 2 sites. Three of the participants were receiving chronic corticosteroid therapy and a stable corticosteroid regimen was to be maintained during the study.

### Pre-assignment

Screening details:

When the Sponsor terminated the study, the participants were told to discontinue ataluren treatment, and to return all unused ataluren to the site for return to the Sponsor. Because of difficulty of traveling to the clinic for these nonambulatory participants, the planned final visits were not performed.

### 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, apple juice, or milk. Study drug dosing was based on milligrams of drug per kilogram of body weight. The dose level for ataluren was 20 milligrams/kilograms (mg/kg) in the morning, 20 mg/kg at midday, and 40 mg/kg in the evening. Administration within 30 minutes after a meal was recommended. Study drug was taken for up to 50 days.

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	6
Received at Least 1 Dose of Study Drug	6
Completed	0
Not completed	6
Study discontinued by Sponsor	6

## Baseline characteristics

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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, apple juice, or milk. Study drug dosing was based on milligrams of drug per kilogram of body weight. The dose level for ataluren was 20 milligrams/kilograms (mg/kg) in the morning, 20 mg/kg at midday, and 40 mg/kg in the evening. Administration within 30 minutes after a meal was recommended. Study drug was taken for up to 50 days.

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Reporting group values	Ataluren	Total	
Number of subjects	6	6	
Age, Customized			
Units: Subjects			
12 to 17 years	3	3	
18 to 20 years	3	3	
Age continuous			
Units: years			
median	17		
full range (min-max)	12 to 20	-	
Sex: Female, Male			
Units: Subjects			
Female	0	0	
Male	6	6	

## 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, apple juice, or milk. Study drug dosing was based on milligrams of drug per kilogram of body weight. The dose level for ataluren was 20 milligrams/kilograms (mg/kg) in the morning, 20 mg/kg at midday, and 40 mg/kg in the evening. Administration within 30 minutes after a meal was recommended. Study drug was taken for up to 50 days.	

### 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:	
A 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 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 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 Adverse Events 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 Day 50	

#### 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	6			
Units: participants				
TEAEs	1			
Treatment Emergent SAEs	0			
AEs Related to Study Treatment	0			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Complete Upper Limb Function Tasks as Measured by the Jebsen Test

End point title	Time to Complete Upper Limb Function Tasks as Measured by the Jebsen Test
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End point description:

Arm and hand function were assessed using the Jebsen test, a standardized clinical evaluation of tasks important to daily living. The test comprises of unilateral subtests performed with each hand (the dominant [DOM] hand and the non-DOM hand): moving and stacking light (250 grams) and heavy (500 grams) objects; picking up small, commonly encountered objects; stacking checkers; simulated feeding; simulated page turning; and writing. Participant performance of each task was timed. Longer time to complete the test indicates worse hand function. Population included all enrolled participants who received at least 1 dose of study drug and with evaluable upper limb function tasks data.

End point type	Secondary
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End point timeframe:

Baseline and Week 6

<b>End point values</b>	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: seconds				
median (full range (min-max))				
Lifting Large Heavy Objects, DOM Hand, Baseline	11 (5 to 120)			
Lifting Large Heavy Objects, DOM Hand, Week 6	10 (9 to 11)			
Lifting Large Heavy Objects, Non-DOM Hand Baseline	11 (5 to 120)			
Lifting Large Heavy Objects, Non-DOM Hand, Week 6	11 (7 to 14)			
Lifting Large Light Objects, DOM Hand, Baseline	9 (4 to 120)			
Lifting Large Light Objects, DOM Hand, Week 6	15 (7 to 22)			
Lifting Large Light Objects, Non-DOM Hand Baseline	7 (3 to 120)			
Lifting Large Light Objects, Non-DOM Hand, Week 6	12 (6 to 18)			
Stacking Large Heavy Objects, DOM Hand, Baseline	118 (10 to 120)			
Stacking Large Heavy Objects, DOM Hand, Week 6	45 (27 to 63)			
Stacking Large Heavy Objects Non-DOM Hand Baseline	120 (28 to 120)			
Stacking Large Heavy Objects, Non-DOM Hand, Week 6	92 (63 to 120)			
Stacking Large Light Objects, DOM Hand, Baseline	69 (5 to 120)			
Stacking Large Light Objects, DOM Hand, Week 6	32 (22 to 42)			
Stacking Large Light Objects Non-DOM Hand Baseline	23 (8 to 120)			
Stacking Large Light Objects, Non-DOM Hand, Week 6	69 (18 to 120)			
Lifting Small Common Objects, DOM Hand, Baseline	16 (7 to 120)			
Lifting Small Common Objects, DOM Hand, Week 6	19 (18 to 19)			
Lifting Small Common Objects Non-DOM Hand Baseline	13 (8 to 120)			
Lifting Small Common Objects, Non-DOM Hand, Week 6	15 (12 to 17)			

Stacking Checkers, DOM Hand, Baseline	7 (4 to 11)			
Stacking Checkers, DOM Hand, Week 6	7 (6 to 7)			
Simulated Feeding, DOM Hand, Baseline	22 (9 to 120)			
Simulated Feeding, DOM Hand, Week 6	40 (15 to 64)			
Simulated Feeding, Non-DOM Hand, Baseline	38 (12 to 120)			
Simulated Feeding, Non-DOM Hand, Week 6	34 (20 to 47)			
Simulated Page Turning, DOM Hand, Baseline	12 (4 to 24)			
Simulated Page Turning, DOM Hand, Week 6	15 (9 to 21)			
Simulated Page Turning, Non-DOM Hand, Baseline	13 (4 to 51)			
Simulated Page Turning, Non-DOM Hand, Week 6	12 (6 to 18)			
Writing, DOM Hand, Baseline	22 (11 to 120)			
Writing, DOM Hand, Week 6	66 (11 to 120)			
Writing, Non-DOM Hand, Baseline	47 (25 to 120)			
Writing, Non-DOM Hand, Week 6	78 (36 to 120)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Upper Limb Function as Measured by the Brooke Upper Extremity Functional Rating Scale

End point title	Upper Limb Function as Measured by the Brooke Upper Extremity Functional Rating Scale
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End point description:

Upper extremity function was assessed using the Brooke Upper Extremity Functional Rating Scale, following standardized procedures. The Brooke Upper Extremity Functional Rating Scale graded arm and shoulder function from 1 to 6, with higher values indicating less function. A rating of "1" was used when the participant was able to abduct his arms in a full circle until they touch above his head, whereas a rating of "6" was used when the participant was unable to raise his hands to his mouth and had no useful function of hands. Population included all enrolled participants who received at least 1 dose of study drug and with evaluable upper limb function tasks data.

End point type	Secondary
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End point timeframe:

Baseline and Week 6

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: score on a scale				
median (full range (min-max))				
Baseline	3 (2 to 5)			
Week 6	3 (3 to 3)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Participant Activities of Daily Living as Assessed Using the Egen Klassifikation (EK) Scale

End point title	Participant Activities of Daily Living as Assessed Using the Egen Klassifikation (EK) Scale
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End point description:

Activities of daily living after loss of ambulation were measured using the EK scale. The EK scale is an ordinal scale ranging from 0 to 30 points where 0 represents the highest level of independent function and 30 the lowest. The scale consists of 10 categories (each scored 0 to 3), involving different functional domains including 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 and arms when eating, 7) ability to turn in bed, 8) ability to cough, 9) ability to speak, and 10) physical well-being. The administration of the EK scale consisted of an interview of the participant to capture how he performs the tasks of daily life (as described by Categories 1 to 9) and how he perceives his wellbeing (as described by Category 10). Population included all enrolled participants who received at least 1 dose of study drug and with evaluable EK Scale data.

End point type	Secondary
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End point timeframe:

Baseline and Week 6

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: score on a scale				
median (full range (min-max))				
Ability to Use Wheelchair, Baseline	2 (2 to 3)			
Ability to Use Wheelchair, Week 6	1 (0 to 2)			
Ability to Transfer From Wheelchair, Baseline	2 (2 to 3)			
Ability to Transfer From Wheelchair, Week 6	2 (2 to 2)			
Ability to Stand, Baseline	3 (1 to 3)			
Ability to Stand, Week 6	2 (1 to 3)			
Ability to Balance in the Wheelchair, Baseline	0 (0 to 3)			
Ability to Balance in the Wheelchair, Week 6	0 (0 to 0)			
Ability to Move Arms, Baseline	2 (0 to 3)			
Ability to Move Arms, Week 6	1 (1 to 1)			
Ability to Use Hands/Arms When Eating, Baseline	2 (1 to 3)			
Ability to Use Hands/Arms When Eating, Week 6	2 (1 to 2)			
Ability to Turn in Bed, Baseline	1 (0 to 3)			

Ability to Turn in Bed, Week 6	1 (0 to 1)			
Ability to Cough, Baseline	0 (0 to 0)			
Ability to Cough, Week 6	0 (0 to 0)			
Ability to Speak, Baseline	0 (0 to 0)			
Ability to Speak, Week 6	0 (0 to 0)			
Physical Well-Being, Baseline	0 (0 to 0)			
Physical Well-Being, Week 6	1 (0 to 1)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Shoulder, Elbow, and Wrist Passive and Active Range of Motion as Measured by Goniometry

End point title	Shoulder, Elbow, and Wrist Passive and Active Range of Motion as Measured by Goniometry
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End point description:

Goniometry was performed to test active and passive range-of motion (RoM) of the left (L) and right (R) shoulder, elbow, and wrist following standardized procedures. The observed angle for passive and active motion for each joint was measured in degrees (0-180). Greater degree of motion indicates better response. Population included all enrolled participants who received at least 1 dose of study drug and with evaluable range of motion data.

End point type	Secondary
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End point timeframe:

Baseline and Week 6

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: degrees				
median (full range (min-max))				
L Elbow Extension, Supine Passive RoM, Baseline	-10 (-20 to 0)			
L Elbow Extension, Supine Passive RoM, Week 6	-15 (-15 to -15)			
R Elbow Extension, Supine Passive RoM, Baseline	-13 (-25 to 0)			
R Elbow Extension, Supine Passive RoM, Week 6	-20 (-20 to -20)			
L Elbow Flexion, Sitting Active RoM, Baseline	115 (0 to 140)			
L Elbow Flexion, Sitting Active RoM, Week 6	-10 (-20 to 0)			
R Elbow Flexion, Sitting Active RoM, Baseline	120 (0 to 140)			
R Elbow Flexion, Sitting Active RoM, Week 6	70 (0 to 140)			
L Elbow Flexion, Supine Passive RoM, Baseline	133 (120 to 140)			
L Elbow Flexion, Supine Passive RoM, Week 6	138 (130 to 145)			

R Elbow Flexion, Supine Passive RoM, Baseline	135 (110 to 140)			
R Elbow Flexion, Supine Passive RoM, Week 6	135 (125 to 145)			
L Shoulder Abduction, Sitting Active RoM, Baseline	18 (0 to 55)			
L Shoulder Abduction, Sitting Active RoM, Week 6	0 (0 to 0)			
R Shoulder Abduction, Sitting Active RoM, Baseline	20 (0 to 70)			
R Shoulder Abduction, Sitting Active RoM, Week 6	5 (0 to 10)			
L Shoulder Abduction, Supine Passive RoM, Baseline	170 (105 to 180)			
L Shoulder Abduction, Supine Passive RoM, Week 6	175 (170 to 180)			
R Shoulder Abduction, Supine Passive RoM, Baseline	180 (120 to 180)			
R Shoulder Abduction, Supine Passive RoM, Week 6	175 (170 to 180)			
L Shoulder Flexion, Sitting Active RoM, Baseline	10 (0 to 45)			
L Shoulder Flexion, Sitting Active RoM, Week 6	10 (0 to 20)			
R Shoulder Flexion, Sitting Active RoM, Baseline	10 (0 to 80)			
R Shoulder Flexion, Sitting Active RoM, Week 6	0 (0 to 0)			
L Shoulder Flexion, Supine Passive RoM, Baseline	165 (160 to 180)			
L Shoulder Flexion, Supine Passive RoM, Week 6	170 (160 to 180)			
R Shoulder Flexion, Supine Passive RoM, Baseline	170 (150 to 180)			
R Shoulder Flexion, Supine Passive RoM, Week 6	175 (170 to 180)			
L Wrist Extension, Sitting Active RoM, Baseline	68 (20 to 80)			
L Wrist Extension, Sitting Active RoM, Week 6	63 (55 to 70)			
R Wrist Extension, Sitting Active RoM, Baseline	65 (30 to 90)			
R Wrist Extension, Sitting Active RoM, Week 6	73 (70 to 75)			
L Wrist Extension, Sitting Passive RoM, Baseline	73 (40 to 100)			
L Wrist Extension, Sitting Passive RoM, Week 6	73 (60 to 85)			
R Wrist Extension, Sitting Passive RoM, Baseline	78 (55 to 90)			
R Wrist Extension, Sitting Passive RoM, Week 6	78 (70 to 85)			
L Wrist Flexion, Sitting Passive RoM, Baseline	75 (35 to 95)			
L Wrist Flexion, Sitting Passive RoM, Week 6	75 (60 to 90)			
R Wrist Flexion, Sitting Passive RoM, Baseline	80 (35 to 90)			
R Wrist Flexion, Sitting Passive RoM, Week 6	68 (45 to 90)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Force Exerted During Elbow Flexion and Extension, Shoulder Abduction, Hand Grip, Key Grip, and Finger Pinch as Assessed by Myometry

End point title	Force Exerted During Elbow Flexion and Extension, Shoulder Abduction, Hand Grip, Key Grip, and Finger Pinch as Assessed by Myometry
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#### End point description:

Upper extremity myometry was performed using a hand-held dynamometer following standardized procedures. Evaluators judged the strength of each muscle using a scoring system. Bilateral assessments were done, and 3 measurements were recorded from each muscle group on each side, when possible. When the measurements were done in duplicate or triplicate, the best value was used. Greater value indicates better measurement. Population included all enrolled participants who received at least 1 dose of study drug and with evaluable myometry data.

End point type	Secondary
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#### End point timeframe:

Baseline and Week 6

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: score on a scale				
median (full range (min-max))				
Left Elbow Extension, Supine, Baseline	12 (2 to 26)			
Left Elbow Extension, Supine, Week 6	16 (14 to 18)			
Right Elbow Extension, Supine, Baseline	12 (1 to 26)			
Right Elbow Extension, Supine, Week 6	15 (13 to 16)			
Left Elbow Flexion, Supine, Baseline	7 (1 to 20)			
Left Elbow Flexion, Supine, Week 6	5 (2 to 7)			
Right Elbow Flexion, Supine, Baseline	7 (0 to 23)			
Right Elbow Flexion, Supine, Week 6	9 (3 to 14)			
Left Finger Pinch, Sitting, Baseline	10 (3 to 20)			
Left Finger Pinch, Sitting, Week 6	6 (2 to 9)			
Right Finger Pinch, Sitting, Baseline	10 (5 to 22)			
Right Finger Pinch, Sitting, Week 6	7 (5 to 8)			
Left Hand Grip, Sitting, Baseline	13 (5 to 23)			
Left Hand Grip, Sitting, Week 6	13 (5 to 20)			
Right Hand Grip, Sitting, Baseline	15 (7 to 34)			
Right Hand Grip, Sitting, Week 6	23 (16 to 29)			
Left Key Grip, Sitting, Baseline	13 (5 to 27)			
Left Key Grip, Sitting, Week 6	15 (8 to 22)			
Right Key Grip, Sitting, Baseline	11 (5 to 24)			

Right Key Grip, Sitting, Week 6	18 (6 to 30)			
Left Shoulder Abduction, Sitting, Baseline	10 (0 to 30)			
Left Shoulder Abduction, Sitting, Week 6	15 (14 to 15)			
Right Shoulder Abduction, Sitting, Baseline	12 (0 to 25)			
Right Shoulder Abduction, Sitting, Week 6	14 (14 to 14)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Complete Hand Fine Motor Coordination and Dexterity Tasks as Measured by 9-Hole Peg Test (9HPT)

End point title	Time to Complete Hand Fine Motor Coordination and Dexterity Tasks as Measured by 9-Hole Peg Test (9HPT)
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End point description:

Hand fine motor coordination and dexterity were assessed using the 9HPT using standardized procedures. The 9HPT is a unilateral test in which 9 pegs were placed in a board and then removed with the dominate and non-dominate hand within a 5-minute time limit. The amount of time required to put the pegs in the holes and remove them again with each hand was recorded. Each test was conducted twice per hand. Longer time to complete the test indicates worse hand fine motor coordination and dexterity. Population included all enrolled participants who received at least 1 dose of study drug and with evaluable 9HPT data.

End point type	Secondary
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End point timeframe:

Baseline and Week 6

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: seconds				
median (full range (min-max))				
Dominant Hand, Baseline	37 (21 to 233)			
Dominant Hand, Week 6	38 (34 to 40)			
Non-Dominant Hand, Baseline	40 (3 to 51)			
Non-Dominant Hand, Week 6	37 (35 to 46)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Forced Vital Capacity (FVC) as Measured by Spirometry

End point title	Forced Vital Capacity (FVC) as Measured by Spirometry
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End point description:

Pulmonary function was assessed as FVC in participants by spirometry using a study-specific spirometer.

Multiple tests were conducted, if needed. Population included all enrolled participants who received at least 1 dose of study drug and with evaluable spirometry data.

End point type	Secondary
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End point timeframe:

Baseline and Week 6

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: liters				
median (full range (min-max))				
Baseline	1 (0.82 to 2.95)			
Week 6	0 (0 to 0)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Systolic and Diastolic Function as Measured by Echocardiography with Tissue Doppler

End point title	Systolic and Diastolic Function as Measured by Echocardiography with Tissue Doppler
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End point description:

Cardiac function was assessed by echocardiography, which included standard parameters (for example, ejection fraction, left ventricle diastolic and systolic dimensions), as well as parameters integrating Doppler flow analysis with imaging to evaluate perturbations in wall motion. A standardized data collection process harmonized data from all participating institutions and allowed for centralized review. Since the study was terminated early, echocardiography data were not collected after the start of study drug administration. Population included all enrolled participants who received at least 1 dose of study drug and with evaluable echocardiography data.

End point type	Secondary
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End point timeframe:

Week 24 and Week 48

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[2]</sup>			
Units: millimeters				
arithmetic mean (standard deviation)				
Week 24	()			
Week 48	()			

Notes:

[2] - Study terminated early and echocardiography data were not collected after start of study drug.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Heart Rate as Assessed by Radial Pulse

End point title | Heart Rate as Assessed by Radial Pulse

End point description:

Heart rate was measured with the radial pulse. Following the Jebsen test, the participant rested for 5 minutes in a sitting position, and the heart rate for the last minute of this rest period was collected as the resting heart rate. Population included all enrolled participants who received at least 1 dose of study drug and with evaluable heart rate data.

End point type | Secondary

End point timeframe:

Baseline and Week 6

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: beats per minute				
median (full range (min-max))				
Baseline	88 (72 to 120)			
Week 6	100 (97 to 102)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Verbal Memory and Attention as Assessed by the Digit Span Task

End point title | Verbal Memory and Attention as Assessed by the Digit Span Task

End point description:

A series of digits (0-9) were presented to the participant in an auditory format only. The task had 2 parts: in the Forward Condition, the participant was requested to repeat back the digits in the order they were presented, and in the Backward Condition, he was requested to reverse the order of presentation. Population included all enrolled participants who received at least 1 dose of study drug and with evaluable verbal memory and attention data. The test was repeated until the participant had 0 correct responses, which was up to 7 times for the Forward Condition and up to 5 times for the Backward Condition at Baseline and at Week 6.

End point type | Secondary

End point timeframe:

Baseline and Week 6

<b>End point values</b>	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: correct responses				
Forward Condition, 1 Correct Response, Baseline	4			
Forward Condition, 1 Correct Response, Week 6	1			
Forward Condition, 2 Correct Responses, Baseline	19			
Forward Condition, 2 Correct Responses, Week 6	4			
Backward Condition, 1 Correct Response, Baseline	4			
Backward Condition, 1 Correct Response, Week 6	2			
Backward Condition, 2 Correct Responses, Baseline	6			
Backward Condition, 2 Correct Responses, Week 6	0			

## Statistical analyses

No statistical analyses for this end point

## Secondary: HRQL as Measured by the PedsQL Inventory Generic Core Scale

End point title	HRQL as Measured by the PedsQL Inventory Generic Core Scale
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End point description:

Health-related quality of life (HRQL) was measured by the Pediatric Quality of Life Inventory (PedsQL) Inventory Generic Core Scale. The generic core module comprised of 23 questions evaluating physical, emotional, social, and school functioning. Examples of items in each of the generic core module scales included: "It is hard for me to run"; "I feel sad or blue"; "I cannot do things that other kids my age can do;" and "It is hard to pay attention in class." Each of the generic core module items was scored on a 5-point response scale from 0 (never a problem) to 4 (almost always a problem). The appropriate age-specific version was completed. PedsQL Inventory Generic Core Scale data at Week 6 is presented. Population included all enrolled participants who received at least 1 dose of study drug and with evaluable PedsQL Inventory Generic Core Scale data at Week 6.

End point type	Secondary
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End point timeframe:

Week 6

<b>End point values</b>	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: units on a scale				
median (full range (min-max))				
Participant-Reported, Health and Activities	4 (0 to 4)			
Participant-Reported, Feelings	1 (0 to 2)			
Participant-Reported, Getting along with Others	2 (0 to 4)			

Participant-Reported, School	1 (0 to 2)			
Parent-Reported, Physical Functioning	4 (0 to 4)			
Parent-Reported, Emotional Functioning	0 (0 to 2)			
Parent-Reported, Social Functioning	1 (0 to 4)			
Parent-Reported, School Functioning	1 (0 to 2)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: HRQL as Measured by the PedsQL Multidimensional Fatigue Scale

End point title	HRQL as Measured by the PedsQL Multidimensional Fatigue Scale
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End point description:

Health-related quality of life (HRQL) was measured by the Pediatric Quality of Life Inventory (PedsQL) Multidimensional Fatigue Scale. The fatigue-specific module comprised of 18 questions evaluating general fatigue, sleep/rest fatigue, and cognitive fatigue. Fatigue-specific module obtains information relating to items such as: "I feel too tired to do things that I like to do"; "I spend a lot of time in bed"; and "I have trouble remembering more than one thing at a time." Each of the fatigue-specific module items was scored on a 5-point response scale from 0 (never a problem) to 4 (almost always a problem). The appropriate age-specific version was completed. PedsQL Multidimensional Fatigue Scale data at Week 6 is presented. Population included all enrolled participants who received at least 1 dose of study drug and with evaluable PedsQL Multidimensional Fatigue Scale data at Week 6.

End point type	Secondary
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End point timeframe:

Week 6

<b>End point values</b>	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: units on a scale				
median (full range (min-max))				
Participant-Reported, General Fatigue	1 (0 to 3)			
Participant-Reported, Sleep/Rest Fatigue	1 (0 to 2)			
Participant-Reported, Cognitive Fatigue	1 (0 to 3)			
Parent-Reported, General Fatigue	1 (0 to 4)			
Parent-Reported, Sleep/Rest Fatigue	0 (0 to 2)			
Parent-Reported, Cognitive Fatigue	1 (0 to 2)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: HRQL as Measured by the INQoL

End point title	HRQL as Measured by the INQoL
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End point description:

HRQL was measured by the Individualized Neuromuscular Quality of Life Questionnaire (INQoL). The INQoL consisted of 45 questions within 10 sections. Four of the sections evaluate key muscle disease symptoms (that is, weakness, locking [myotonia], pain, and fatigue), 5 sections evaluate the degree and importance of the impact of muscle disease on particular areas of life, and 1 section asks about the positive and negative effects of treatment. A higher score indicates greater symptom impact or worse HRQL, with a range of 0-7. Since the study was terminated early, INQoL data were not collected. Population included all enrolled participants who received at least 1 dose of study drug and with evaluable INQoL data.

End point type	Secondary
End point timeframe:	Week 24 and Week 48

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[3]</sup>			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 24	( )			
Week 48	( )			

Notes:

[3] - Study terminated early and INQoL data were not collected.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Muscle Fragility as Determined by Serum Creatine Kinase (CK) Levels

End point title	Muscle Fragility as Determined by Serum Creatine Kinase (CK) Levels
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End point description:

Blood samples collected for chemistry assays were used to quantify serum CK concentrations. Serum CK was assessed as a potential biomarker for muscle fragility, with a reduction in serum CK considered to be a positive outcome. The reference range was based on the age of the participant. Population included all enrolled participants who received at least 1 dose of study drug and with evaluable CK data.

End point type	Secondary
End point timeframe:	Baseline and Week 6

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: units/liter (U/L)				
median (full range (min-max))				
CK Levels (Reference Range 18-198 U/L), Baseline	1217 (614 to 2136)			
CK Levels (Reference Range 18-198 U/L), Week 6	764 (764 to 764)			

CK Levels (Reference Range 18-363 U/L), Baseline	2605 (1413 to 3797)			
CK Levels (Reference Range 18-363 U/L), Week 6	0 (0 to 0)			
CK Levels (Reference Range 18-408 U/L), Baseline	2343 (2343 to 2343)			
CK Levels (Reference Range 18-408 U/L), Week 6	2753 (2753 to 2753)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Gastrocnemius Muscle Dystrophin Expression as Determined by Immunofluorescence or by Western Blotting Techniques

End point title	Gastrocnemius Muscle Dystrophin Expression as Determined by Immunofluorescence or by Western Blotting Techniques
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End point description:

The gastrocnemius muscle was to be biopsied from 1 leg to assess for the production of dystrophin at Week 36. The production of dystrophin was to be measured by immunofluorescence staining of the sarcolemmal membrane or by Western blotting techniques with an antibody to the C-terminal portion of the dystrophin protein (excluding revertant fibers). Since the study was terminated early, gastrocnemius muscle dystrophin expression data were not collected after the start of study drug administration. Population included all enrolled participants who received at least 1 dose of study drug and with evaluable dystrophin production data.

End point type	Secondary
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End point timeframe:

Week 36

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[4]</sup>			
Units: percent of cells				
arithmetic mean (standard deviation)	( )			

Notes:

[4] - Study terminated early. Data for this outcome measure were not collected after start of study drug.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Study Drug Compliance

End point title	Study Drug Compliance
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End point description:

Study drug compliance was assessed by the participant daily diary and quantification of used and unused study drug. Compliance was assessed in terms of the amount of drug actually taken relative to the amount that should have been taken during the study. Population included all enrolled participants who received at least 1 dose of study drug and with evaluable study drug compliance data.

End point type	Secondary
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End point timeframe:

Baseline to Day 50

<b>End point values</b>	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: participants				
Missed 0 Doses	1			
Missed 1 Dose	2			
Missed 2 Doses	0			
Missed 3 Doses	0			
Missed 4 Doses	1			
Missed >5 Doses	0			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetics: Ataluren Plasma Exposure

End point title	Pharmacokinetics: Ataluren Plasma Exposure
End point description:	Blood for ataluren concentrations over a 24-hour period was to be collected on Days 2 and 3 of Week 6. Analysis of the blood samples was to be conducted using a validated high performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) method. Since the study was terminated early, steady state data were not collected at Week 6. Population included all enrolled participants who received at least 1 dose of study drug and with evaluable plasma data.
End point type	Secondary
End point timeframe:	0, 2, 3, 6, 8, 9, 12, 14, 15, and 24 hours after the morning dose

<b>End point values</b>	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[5]</sup>			
Units: microgram/milliliters (µg/mL)				
arithmetic mean (standard deviation)	( )			

Notes:

[5] - Since the study was terminated early, steady state data were not collected at Week 6.

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to Day 50

Assessment type	Systematic
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### Dictionary used

Dictionary name	11.1
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Dictionary version	11.1
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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, apple juice, or milk. Study drug dosing was based on milligrams of drug per kilogram of body weight. The dose level for ataluren was 20 mg/kg in the morning, 20 mg/kg at midday, and 40 mg/kg in the evening. Administration within 30 minutes after a meal was recommended. Study drug was taken for up to 50 days.

<b>Serious adverse events</b>	Ataluren		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	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	1 / 6 (16.67%)		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Infections and infestations			
Nasopharyngitis			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported