Clinical trial results:
Phase 2, Non-Interventional, Clinical Study to Assess Dystrophin Levels in Subjects With Nonsense Mutation Duchenne Muscular Dystrophy who Have Been Treated With Ataluren for 9 Months

Summary

EudraCT number	2019-001691-11
Trial protocol	Outside EU/EEA
Global end of trial date	03 June 2019

Results information

Result version number	v1 (current)
This version publication date	20 May 2022
First version publication date	20 May 2022

Trial information

Trial identification

Sponsor protocol code	PTC124-GD-046-DMD

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03796637
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	PTC Therapeutics, Inc.
Sponsor organisation address	100 Corporate Court, South Plainfield, United States, NJ 07080
Public contact	Medical Information, PTC Therapeutics, Inc., +011 44 1-866-562-4620, medinfo@ptcbio.com
Scientific contact	Medical Information, PTC Therapeutics International Limited, +353 19068700, medinfo@ptcbio.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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	03 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 June 2019
Global end of trial reached?	Yes
Global end of trial date	03 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to assess the levels of dystrophin in ambulatory participants with nonsense mutation duchenne muscular dystrophy (nmDMD) currently being treated with ataluren for ≥9 months using a quantitative electrochemiluminescence (ECL) assay.

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 2013) and in conformance with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) guidance documents.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 April 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

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)	4
Adolescents (12-17 years)	2
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Six ambulatory male participants with nmDMD who had been receiving ataluren were enrolled and treated in this study.

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 who had been receiving ataluren, were dosed daily 10 milligrams (mg)/kilogram (kg) in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening, for ≥9 months from ongoing PTC-sponsored nmDMD clinical trials.

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

Dosage and administration details:

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

Number of subjects in period 1	Ataluren
Started	6
Completed	6

Baseline characteristics

Reporting groups	
Reporting group title	Ataluren
Reporting group description:	
Participants who had been receiving ataluren, were dosed daily 10 milligrams (mg)/kilogram (kg) in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening, for ≥9 months from ongoing PTC-sponsored nmDMD clinical trials.	

Reporting group values	Ataluren	Total	
Number of subjects	6	6	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	4	4	
Adolescents (12-17 years)	2	2	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	10.2		
standard deviation	± 2.04	-	
Sex: Female, Male Units: participants			
Female	0	0	
Male	6	6	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	6	6	
Unknown or Not Reported	0	0	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	6	6	
More than one race	0	0	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Ataluren

Reporting group description:

Participants who had been receiving ataluren, were dosed daily 10 milligrams (mg)/kilogram (kg) in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening, for ≥9 months from ongoing PTC-sponsored nmDMD clinical trials.

Primary: Mean Dystrophin Levels as Measured by Electrochemiluminescence (ECL)

End point title	Mean Dystrophin Levels as Measured by Electrochemiluminescence (ECL)[1]

End point description:

The mean dystrophin protein levels were measured by ECL. Dystrophin levels are reported by muscle group (gastrocnemius, tibialis anterior, and across muscle locations). Results below the limit of quantitation were imputed as half of lower limit of quantitation (LLOQ). LLOQ = 0.5 micrograms (µg)/milliliter (mL). Intent-to-treat (ITT) population included all enrolled participants with a valid assessment of dystrophin level, as measured by ECL.

End point type	Primary

End point timeframe:

Day 1 of biopsy

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 analysis was not planned for this endpoint.

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: nanograms (ng)/mg				
arithmetic mean (standard deviation)				
Gastrocnemius	0.0844 (± 0.05874)			
Tibialis Anterior	0.1002 (± 0.08060)			
Across Muscle Locations	0.1054 (± 0.08300)			

Statistical analyses

No statistical analyses for this end point

Secondary: Dystrophin Protein Levels as Determined by Immunohistochemistry

End point title	Dystrophin Protein Levels as Determined by Immunohistochemistry

End point description:

Dystrophin levels by IHC mean membrane stain density are reported by muscle group (gastrocnemius, tibialis anterior, and across muscle locations). ITT population included all enrolled participants with a valid assessment of dystrophin level, as measured by ECL.

End point type	Secondary

End point timeframe:

Day 1 of biopsy

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ng/mg				
arithmetic mean (standard deviation)				
Gastrocnemius	0.28817 (± 0.220547)			
Tibialis Anterior	0.26578 (± 0.226510)			
Across Muscle Locations	0.30483 (± 0.218600)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline (Day 1) up to Week 1	
Adverse event reporting additional description:	
Safety population included all participants who received at least 1 dose of ataluren.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups	
Reporting group title	Ataluren
Reporting group description:	
Participants who had been receiving ataluren, were dosed daily 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening, for ≥9 months from ongoing PTC-sponsored nmDMD clinical trials.	

Serious adverse events	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			

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	2 / 6 (33.33%)		
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
General disorders and administration site conditions			
Puncture site discharge			
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? Yes

Date	Amendment
20 March 2019	The overall reason for the amendment was to ensure that sufficient muscle tissue for analysis was obtained from the biopsy procedure.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported