Clinical trial results:
An Open-Label Study Evaluating the Safety and Pharmacokinetics of Ataluren in Children From 6 Months to <2 Years of Age with Nonsense Mutation Duchenne Muscular Dystrophy

Summary

EudraCT number	2020-000980-21
Trial protocol	Outside EU/EEA
Global end of trial date	07 August 2023

Results information

Result version number	v2 (current)
This version publication date	20 April 2024
First version publication date	23 February 2024
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	PTC124-GD-048-DMD

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04336826
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000115-PIP01-07
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	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	07 August 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 August 2023
Global end of trial reached?	Yes
Global end of trial date	07 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial was to assess the safety and tolerability of ataluren in male children with nonsense mutation Duchenne muscular dystrophy (nmDMD) aged ≥6 months to <2 years old.

Protection of trial subjects:

This study was designed and monitored in accordance with PTC Therapeutics (PTC) procedures, which comply with the ethical principles of Good Clinical Practices (GCP) as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 December 2021
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)	6
Children (2-11 years)	0
Adolescents (12-17 years)	0
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:

A total of 6 participants were screened and enrolled into the 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 received ataluren oral suspension 10 milligrams (mg)/kilogram (kg) in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening each day for up to 24 weeks.

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

Dosage and administration details:

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

Number of subjects in period 1	Ataluren
Started	6
Received at least 1 dose of study drug	6
Completed	6

Baseline characteristics

Reporting groups	
Reporting group title	Ataluren
Reporting group description:	
Participants received ataluren oral suspension 10 milligrams (mg)/kilogram (kg) in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening each day for up to 24 weeks.	

Reporting group values	Ataluren	Total	
Number of subjects	6	6	
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	1.153		
standard deviation	± 0.4485	-	
Sex: Female, Male Units: participants			
Female	0	0	
Male	6	6	
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	5	5	
More than one race	1	1	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	1	
Not Hispanic or Latino	5	5	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Ataluren

Reporting group description:

Participants received ataluren oral suspension 10 milligrams (mg)/kilogram (kg) in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening each day for up to 24 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) was as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. Serious adverse event (SAE): an AE that met at least 1 of the following criteria: resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions, congenital anomaly/birth defect, important medical event. A TEAE was defined as an AE that occurred or worsened while on ataluren (on or after first dose of ataluren) up to 4 weeks after the last dose. A summary of all SAEs and Other AEs (nonserious) regardless of causality is located in the 'Reported Adverse Events' Section. Safety analysis set included all participants who received at least 1 dose of ataluren.

End point type	Primary

End point timeframe:

Baseline up to Week 28

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: The analysis was descriptive in nature.

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: participants	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Concentration (Ctrough) of Ataluren

End point title	Trough Concentration (Ctrough) of Ataluren

End point description:

PK population included all participants who received at least 1 dose of ataluren and had 1 PK concentration datum. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Predose up to 12 hours postdose at Week 24

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: µg/mL				
arithmetic mean (standard deviation)	3.48 (± 3.36)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Concentration (Cmax) of Ataluren

End point title	Maximum Concentration (Cmax) of Ataluren

End point description:

PK population included all participants who received at least 1 dose of ataluren and had 1 PK concentration datum.

End point type	Secondary

End point timeframe:

Predose up to 12 hours postdose at Week 24

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: µg/mL				
arithmetic mean (standard deviation)	12.6 (± 3.64)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Maximum Plasma Concentration (Tmax) of Ataluren

End point title	Time to Maximum Plasma Concentration (Tmax) of Ataluren

End point description:

PK population included all participants who received at least 1 dose of ataluren and had 1 PK concentration datum.

End point type	Secondary

End point timeframe:

Predose up to 12 hours postdose at Week 24

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hours				
median (full range (min-max))	2.08 (1.00 to 4.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-Time Curve From Time 0 to 24 Hours (AUC0-24) of Ataluren

End point title	Area Under the Concentration-Time Curve From Time 0 to 24 Hours (AUC0-24) of Ataluren

End point description:

Pharmacokinetic (PK) population included all participants who received at least 1 dose of ataluren and had 1 PK concentration datum. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Predose up to 12 hours postdose at Week 24

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: hours*micrograms (µg)/milliliter (mL)				
arithmetic mean (standard deviation)	167 (± 23.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-Time Curve Between Dosing Interval (AUC0-τ) of Ataluren

End point title	Area Under the Concentration-Time Curve Between Dosing Interval (AUC0-τ) of Ataluren

End point description:

PK population included all participants who received at least 1 dose of ataluren and had 1 PK concentration datum. Here, '99999' represents "Per prespecified analysis, 'Measure Type' and 'Method of Dispersion' were not estimable for this outcome measure because there were insufficient number of

participants with data within the linear regression of concentration in the logarithmic scale versus time."

End point type	Secondary

End point timeframe:

Predose up to 12 hours postdose at Week 24

End point values	Ataluren			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hours*µg/mL				
arithmetic mean (standard deviation)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to Week 28	
Adverse event reporting additional description:	
Safety analysis set included all participants who received at least 1 dose of ataluren.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups	
Reporting group title	Ataluren
Reporting group description:	
Participants received ataluren oral suspension 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening each day for up to 24 weeks.	

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	5 / 6 (83.33%)		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Teething			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Skin plaque			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Infections and infestations			
Body tinea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Enterovirus infection			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Otitis media			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Upper respiratory tract infection			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
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
29 April 2021	It included following changes: • The duration of treatment was changed from "52 weeks" to "24 weeks" and the end of treatment (EOT) timepoint was updated to occur at Week 24 instead of Week 52. • Removal of the efficacy endpoint (change in motor development). • Removal of the exploratory endpoint "abnormalities of physical findings, clinical laboratory tests, or electrocardiograms (ECGs)" since this information is captured as part of the primary endpoint. • The exploratory objective of "to assess changes from baseline in creatine kinase (CK) levels after 24 weeks of ataluren treatment" and the exploratory endpoint of "change from baseline in CK levels" were added. • Updates were made to the volume and process by which blood PK samples are collected.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported