Clinical trial results:
CNS Unmet Medical Need in Mucopolysaccharidosis: A Phase 2 Safety and Pharmacokinetics Study of Ataluren (COMPASS)

Summary

EudraCT number	2014-002596-28
Trial protocol	DE GB
Global end of trial date	20 July 2017

Results information

Result version number	v1 (current)
This version publication date	31 March 2018
First version publication date	31 March 2018

Trial information

Trial identification

Sponsor protocol code	PTC124-GD-024-MPS

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	Joseph McIntosh, MD, PTC Therapeutics Inc., 1 908-912-9138,
Scientific contact	Joseph McIntosh, MD, PTC Therapeutics Inc., 1 908-912-9138,

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	13 September 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 July 2017
Global end of trial reached?	Yes
Global end of trial date	20 July 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the studies were to:
- Characterize the safety profile of ataluren in patients with nonsense mutation mucopolysaccharidosis type 1 (nmMPS 1), and
- Evaluate the cerebrospinal fluid (CSF) and plasma pharmacokinetics (PK) of ataluren in patients with nmMPS 1.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 September 2015
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	Germany: 3
Worldwide total number of subjects	3
EEA total number of subjects	3

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)	2
Adolescents (12-17 years)	1
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:

The study included a 14-day screening period.

Period 1

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

Arms

Arm title	"Non-treated Patients" (Period 1)

Arm description:

All patients participated in treatment Period 1 and received 12 weeks of ataluren.
Patients who were to be enrolled included:
- patients on enzyme replacement therapy (ERT) at study entry (referred to as “ERT patients”),
- patients not on ERT at study entry but who had previously received bone marrow transplantation/hematopoietic stem cell transplantation (BMT/HSCT) (referred to as “post-BMT/HSCT patients”), and
- patients not on ERT at study entry and who had not previously received BMT/HSCT (referred to as “non-treated patients”).
In this study, the 3 patients enrolled were in the "non-treated" arm, and no "ERT" or "post-BMT/HSCT" patients were enrolled.

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

Dosage and administration details:

Ataluren was administered 3 times a day: 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening; during 12 weeks.

Number of subjects in period 1	"Non-treated Patients" (Period 1)
Started	3
Completed	3

Baseline characteristics

Reporting groups	
Reporting group title	All patients

Reporting group description: -

Reporting group values	All patients	Total	
Number of subjects	3	3	
Age categorical Units: Subjects			
Children (2-11 years)	2	2	
Adolescents (12-17 years)	1	1	
Gender categorical Units: Subjects			
Female	1	1	
Male	2	2	

End points

End points reporting groups

Reporting group title	"Non-treated Patients" (Period 1)

Reporting group description:

All patients participated in treatment Period 1 and received 12 weeks of ataluren.
Patients who were to be enrolled included:
- patients on enzyme replacement therapy (ERT) at study entry (referred to as "ERT patients"),
- patients not on ERT at study entry but who had previously received bone marrow transplantation/hematopoietic stem cell transplantation (BMT/HSCT) (referred to as "post-BMT/HSCT patients"), and
- patients not on ERT at study entry and who had not previously received BMT/HSCT (referred to as "non-treated patients").
In this study, the 3 patients enrolled were in the "non-treated" arm, and no "ERT" or "post-BMT/HSCT" patients were enrolled.

Primary: Ataluren Cerebrospinal Fluid Concentrations

End point title	Ataluren Cerebrospinal Fluid Concentrations[1]

End point description:

End point type	Primary

End point timeframe:

Week 12

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: Descriptive statistics only due to the small number of patients in the study. General conclusions regarding the safety and PK of ataluren in patients with nmMPS 1 cannot be made. The results of this study indicate that ataluren crosses the blood-brain barrier.

End point values	"Non-treated Patients" (Period 1)			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: nanogram(s)/millilitre				
arithmetic mean (standard deviation)				
Pre-dose	79.40 (± 87.116)			

Statistical analyses

No statistical analyses for this end point

Primary: Ataluren Plasma Concentrations

End point title	Ataluren Plasma Concentrations[2]

End point description:

End point type	Primary

End point timeframe:

Week 12

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: Descriptive statistics only due to the small number of patients in the study. General conclusions regarding the safety and PK of ataluren in patients with nmMPS 1 cannot be made.

End point values	"Non-treated Patients" (Period 1)			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: microgram(s)/millilitre				
arithmetic mean (standard deviation)				
Pre-dose	4.023 (± 2.4918)			
Hour 2	10.297 (± 1.3580)			
Hour 4	4.720 (± 1.2210)			
Hour 6	2.940 (± 0.4530)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From Baseline to Week 12	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0
Reporting groups	
Reporting group title	Safety Population

Reporting group description: -

Serious adverse events	Safety Population		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Safety Population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
Investigations			
Weight increased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Gastrointestinal disorders			
Flatulence			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Infections and infestations			

Rash pustular subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1 1 / 3 (33.33%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 December 2015	· Secondary Objectives and endpoints were modified to delete the urinary glycosaminoglycan (GAG) level assessed by the conventional method and the urine filter paper method. · Several inclusion and exclusion criteria were amended to ensure consistency throughout the protocol. · The schedule of assessments was updated. · The Metabolic Urinary GaG value was updated.

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.

PTC124-GD-024-MPS was terminated early due to low enrolment. Due to the small number of patients in the study, general conclusions regarding the safety and PK of ataluren in patients with nmMPS 1 cannot be made.

Notes: