Clinical trial results:
A Phase 2, Multicenter, Randomized, Double-Masked, Placebo-Controlled Study of the Safety and Efficacy of Ataluren (PTC124) for the Treatment of Nonsense Mutation Aniridia

Summary

EudraCT number	2022-001013-39
Trial protocol	Outside EU/EEA
Global end of trial date	22 January 2021

Results information

Result version number	v1 (current)
This version publication date	16 July 2022
First version publication date	16 July 2022

Trial information

Trial identification

Sponsor protocol code	PTC124-GD-028 ANI

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02647359
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	22 January 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 January 2021
Global end of trial reached?	Yes
Global end of trial date	22 January 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the effect of ataluren on Maximum Reading Speed as measured using the Minnesota Low Vision Reading Test (MNREAD) Acuity Charts in participants with nonsense mutation aniridia.

Protection of trial subjects:

The study was conducted in full accordance with the Declaration of Helsinki and the International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Consolidated Guideline (E6), and any applicable national and local laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 January 2016
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	Canada: 5
Country: Number of subjects enrolled	United States: 34
Worldwide total number of subjects	39
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)	18
Adolescents (12-17 years)	10
Adults (18-64 years)	11
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 44 participants were screened and 39 were randomized to either ataluren or placebo arm.

Period 1

Period 1 title	Stage 1: Double-Masked Period (48 Weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Ataluren

Arm description:

Participants received ataluren orally 3 times a day (TID) at a dose of 10 milligrams (mg)/kilogram (kg) in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for 48 weeks in Stage 1 (double-masked period) and for additional 96 weeks in Stage 2 (open-label extension period). Participants, who completed Stage 2 and agreed to continue in open-label sub-study, continued to receive ataluren treatment at same dose as mentioned above, for 96 weeks.

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

Dosage and administration details:

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

Arm title	Placebo

Arm description:

Participants received placebo matched to ataluren TID orally in the morning, at midday, and in the evening for 48 weeks in Stage 1 (double-masked period) and ataluren orally TID at a dose of 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for additional 96 weeks in Stage 2 (open-label extension period). Participants, who completed Stage 2 and agreed to continue in open-label sub-study, continued to receive ataluren treatment at same dose as mentioned above, for 96 weeks.

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

Dosage and administration details:

Placebo matched to ataluren was administered per schedule specified in the arm description.

Number of subjects in period 1	Ataluren	Placebo
Started	26	13
Received at least 1 dose of study drug	26	13
Completed	22	12
Not completed	4	1
Non-compliance with study drug	-	1
Other than specified	4	-

Period 2

Period 2 title	Stage 2: Open-Label Extension (96 Weeks)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Ataluren

Arm description:

Participants received ataluren orally 3 times a day (TID) at a dose of 10 milligrams (mg)/kilogram (kg) in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for 48 weeks in Stage 1 (double-masked period) and for additional 96 weeks in Stage 2 (open-label extension period). Participants, who completed Stage 2 and agreed to continue in open-label sub-study, continued to receive ataluren treatment at same dose as mentioned above, for 96 weeks.

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

Dosage and administration details:

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

Arm title	Placebo

Arm description:

Participants received placebo matched to ataluren TID orally in the morning, at midday, and in the evening for 48 weeks in Stage 1 (double-masked period) and ataluren orally TID at a dose of 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for additional 96 weeks in Stage 2 (open-label extension period). Participants, who completed Stage 2 and agreed to continue in open-label sub-study, continued to receive ataluren treatment at same dose as mentioned above, for 96 weeks.

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

Dosage and administration details:

Placebo matched to ataluren was administered per schedule specified in the arm description.

Number of subjects in period 2[1]	Ataluren	Placebo
Started	22	11
Completed	12	7
Not completed	10	4
Adverse event, non-fatal	2	1
Other than specified	8	3

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 1 participant in placebo arm completed Stage 1 but did not enter open-label part

Period 3

Period 3 title	Open-Label Sub-Study (96 Weeks)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Ataluren

Arm description:

Participants received ataluren orally 3 times a day (TID) at a dose of 10 milligrams (mg)/kilogram (kg) in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for 48 weeks in Stage 1 (double-masked period) and for additional 96 weeks in Stage 2 (open-label extension period). Participants, who completed Stage 2 and agreed to continue in open-label sub-study, continued to receive ataluren treatment at same dose as mentioned above, for 96 weeks.

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

Dosage and administration details:

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

Arm title	Placebo

Arm description:

Participants received placebo matched to ataluren TID orally in the morning, at midday, and in the evening for 48 weeks in Stage 1 (double-masked period) and ataluren orally TID at a dose of 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for additional 96 weeks in Stage 2 (open-label extension period). Participants, who completed Stage 2 and agreed to continue in open-label sub-study, continued to receive ataluren treatment at same dose as mentioned above, for 96 weeks.

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

Dosage and administration details:

Placebo matched to ataluren was administered per schedule specified in the arm description.

Number of subjects in period 3[2]	Ataluren	Placebo
Started	10	7
Completed	2	3
Not completed	8	4
Other than specified	7	4
Lost to follow-up	1	-

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 1 participant in placebo arm completed Stage 1 but did not enter open-label part

Baseline characteristics

Reporting groups

Reporting group title	Ataluren

Reporting group description:

Participants received ataluren orally 3 times a day (TID) at a dose of 10 milligrams (mg)/kilogram (kg) in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for 48 weeks in Stage 1 (double-masked period) and for additional 96 weeks in Stage 2 (open-label extension period). Participants, who completed Stage 2 and agreed to continue in open-label sub-study, continued to receive ataluren treatment at same dose as mentioned above, for 96 weeks.

Reporting group title	Placebo

Reporting group description:

Participants received placebo matched to ataluren TID orally in the morning, at midday, and in the evening for 48 weeks in Stage 1 (double-masked period) and ataluren orally TID at a dose of 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for additional 96 weeks in Stage 2 (open-label extension period). Participants, who completed Stage 2 and agreed to continue in open-label sub-study, continued to receive ataluren treatment at same dose as mentioned above, for 96 weeks.

Reporting group values	Ataluren	Placebo	Total
Number of subjects	26	13	39
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	14.1	19.2	
standard deviation	± 10.12	± 19.43	-
Sex: Female, Male Units: participants			
Female	10	8	18
Male	16	5	21
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	3	2	5
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	22	11	33
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	26	12	38
Unknown or Not Reported	0	0	0

Subject analysis sets

Subject analysis set title	Stage 1: Ataluren
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received ataluren orally TID at a dose of 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for 48 weeks in Stage 1 (double-masked period).

Subject analysis set title	Stage 1: Placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received placebo matched to ataluren TID orally in the morning, at midday, and in the evening for 48 weeks in Stage 1 (double-masked period).

Subject analysis set title	Overall Ataluren Exposure
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received ataluren orally TID at a dose of 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for 48 weeks in Stage 1 (double-masked period) and for additional 96 weeks in Stage 2 (open-label extension period). Participants, who completed Stage 2 and agreed to continue in open-label sub-study, continued to receive ataluren treatment at same dose as mentioned above, for 96 weeks.

Reporting group values	Stage 1: Ataluren	Stage 1: Placebo	Overall Ataluren Exposure
Number of subjects	26	13	37
Age categorical Units: Subjects			
Age Continuous Units: years arithmetic mean standard deviation	 22 ±	 10 ±	 35 ±
Sex: Female, Male Units: participants			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			

End points

End points reporting groups

Reporting group title	Ataluren

Reporting group description:

Participants received ataluren orally 3 times a day (TID) at a dose of 10 milligrams (mg)/kilogram (kg) in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for 48 weeks in Stage 1 (double-masked period) and for additional 96 weeks in Stage 2 (open-label extension period). Participants, who completed Stage 2 and agreed to continue in open-label sub-study, continued to receive ataluren treatment at same dose as mentioned above, for 96 weeks.

Reporting group title	Placebo

Reporting group description:

Participants received placebo matched to ataluren TID orally in the morning, at midday, and in the evening for 48 weeks in Stage 1 (double-masked period) and ataluren orally TID at a dose of 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for additional 96 weeks in Stage 2 (open-label extension period). Participants, who completed Stage 2 and agreed to continue in open-label sub-study, continued to receive ataluren treatment at same dose as mentioned above, for 96 weeks.

Reporting group title	Ataluren

Reporting group description:

Participants received ataluren orally 3 times a day (TID) at a dose of 10 milligrams (mg)/kilogram (kg) in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for 48 weeks in Stage 1 (double-masked period) and for additional 96 weeks in Stage 2 (open-label extension period). Participants, who completed Stage 2 and agreed to continue in open-label sub-study, continued to receive ataluren treatment at same dose as mentioned above, for 96 weeks.

Reporting group title	Placebo

Reporting group description:

Participants received placebo matched to ataluren TID orally in the morning, at midday, and in the evening for 48 weeks in Stage 1 (double-masked period) and ataluren orally TID at a dose of 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for additional 96 weeks in Stage 2 (open-label extension period). Participants, who completed Stage 2 and agreed to continue in open-label sub-study, continued to receive ataluren treatment at same dose as mentioned above, for 96 weeks.

Reporting group title	Ataluren

Reporting group description:

Participants received ataluren orally 3 times a day (TID) at a dose of 10 milligrams (mg)/kilogram (kg) in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for 48 weeks in Stage 1 (double-masked period) and for additional 96 weeks in Stage 2 (open-label extension period). Participants, who completed Stage 2 and agreed to continue in open-label sub-study, continued to receive ataluren treatment at same dose as mentioned above, for 96 weeks.

Reporting group title	Placebo

Reporting group description:

Participants received placebo matched to ataluren TID orally in the morning, at midday, and in the evening for 48 weeks in Stage 1 (double-masked period) and ataluren orally TID at a dose of 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for additional 96 weeks in Stage 2 (open-label extension period). Participants, who completed Stage 2 and agreed to continue in open-label sub-study, continued to receive ataluren treatment at same dose as mentioned above, for 96 weeks.

Subject analysis set title	Stage 1: Ataluren
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received ataluren orally TID at a dose of 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for 48 weeks in Stage 1 (double-masked period).

Subject analysis set title	Stage 1: Placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received placebo matched to ataluren TID orally in the morning, at midday, and in the evening for 48 weeks in Stage 1 (double-masked period).

Subject analysis set title	Overall Ataluren Exposure
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received ataluren orally TID at a dose of 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for 48 weeks in Stage 1 (double-masked period) and for additional 96 weeks in Stage 2 (open-label extension period). Participants, who completed Stage 2 and agreed to continue in open-label sub-study, continued to receive ataluren treatment at same dose as mentioned above, for 96 weeks.

Primary: Percent Change From Baseline in Maximum Reading Speed of Oculus Unitas (OU) (Both Eyes) at Week 48, as Measured Using the Minnesota Low Vision Reading Test (MNREAD) Acuity Charts

End point title	Percent Change From Baseline in Maximum Reading Speed of Oculus Unitas (OU) (Both Eyes) at Week 48, as Measured Using the Minnesota Low Vision Reading Test (MNREAD) Acuity Charts

End point description:

MNREAD Acuity Chart test consists of short sentences with print size decreasing by 0.1 log unit steps from a maximum of 1.3 logarithm of the minimum angle of resolution (logMAR) (equivalent to 20/400 or 6/120 when viewed at 40 centimeters [cm]) to −0.5 logMAR (equivalent to 20/6 or 6/2). MNREAD Acuity Chart curve of reading speed vs print size has a typical shape for normally sighted persons and many low-vision individuals. This curve is characterized by 3 summary values. At large print sizes, reading speed remains fairly constant, forming a plateau that represents the maximum reading speed. As print size decreases, a critical print size (CPS) is reached at which reading speed begins to decline rapidly. Finally, the smallest print size that can be read is defined as reading acuity (RA). Intent-to-treat (ITT) population included all randomized participants who received at least 1 dose of study drug. 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Week 48

End point values	Ataluren	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	5		
Units: percent change				
least squares mean (standard error)	9.87 (± 7.425)	-0.89 (± 11.809)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed using analysis of covariance (ANCOVA) with age and baseline Maximum Reading Speed (both eyes) as covariates, and treatment as a factor.

Comparison groups	Ataluren v Placebo
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4868 [1]
Method	ANCOVA
Parameter estimate	Least Square (LS) Mean Difference
Point estimate	10.76

Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.914
upper limit	43.434

Notes:

[1] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Reading Accessibility Index of Both Eyes at Week 48

End point title	Change From Baseline in Reading Accessibility Index of Both Eyes at Week 48

End point description:

Reading Accessibility Index is defined as the mean reading speed in words per minute (wpm) across the 10 largest physical print sizes on the MNREAD Acuity Chart, normalized by the value for a group of normally sighted young adults. For a viewing distance of 40 cm, this range of print sizes corresponds to 0.4 to 1.3 logMAR. Because the Reading Accessibility Index is normalized by the value for a group of normally sighted young adults (aged 18 to 39 years), a Reading Accessibility Index of 1.0 represents normal performance for this age group. Values less than 1.0 mean reduced accessibility to printed text within the range of print size encountered in daily life. Missing data was imputed using last observation carried forward (LOCF) method. ITT population included all randomized participants who received at least 1 dose of study drug. 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Ataluren	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	6		
Units: units on a scale				
arithmetic mean (standard deviation)	0.10 (± 0.241)	0.02 (± 0.267)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Best Corrected Visual Acuity (BCVA) at Week 48

End point title	Change From Baseline in Best Corrected Visual Acuity (BCVA) at Week 48

End point description:

The BCVA was evaluated using the Early Treatment Diabetic Retinopathy Study (ETDRS) Method. Missing data was imputed using LOCF method. The ITT population included all randomized participants who received at least 1 dose of study drug. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint. 'n' = participants evaluable for specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Ataluren	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	13		
Units: LogMAR				
arithmetic mean (standard deviation)				
Left Eye (n = 22, 13)	-0.00 (± 0.076)	0.01 (± 0.103)		
Right Eye (n = 24, 13)	0.03 (± 0.125)	-0.04 (± 0.138)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Maximum Reading Speed of Oculus Dexter (OD) (Right Eye) and Oculus Sinister (OS) (Left Eye) at Week 48

End point title	Percent Change From Baseline in Maximum Reading Speed of Oculus Dexter (OD) (Right Eye) and Oculus Sinister (OS) (Left Eye) at Week 48

End point description:

MNREAD Acuity Chart test consists of short sentences with print size decreasing by 0.1 log unit steps from a maximum of 1.3 logMAR (equivalent to 20/400 or 6/120 when viewed at 40 cm) to −0.5 logMAR (equivalent to 20/6 or 6/2). An MNREAD Acuity Chart curve of reading speed vs print size has a typical shape for normally sighted persons and many low-vision individuals. This curve is characterized by 3 summary values. At large print sizes, reading speed remains fairly constant, forming a plateau that represents the maximum reading speed. As the print size decreases, a CPS is reached at which reading speed begins to decline rapidly. Finally, the smallest print size that can be read is defined as the RA. The ITT population included all randomized participants who received at least 1 dose of study drug. 'Overall number of participants analyzed' = participants evaluable for this endpoint. 'n' = participants evaluable for specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Ataluren	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	6		
Units: percent change				
arithmetic mean (standard deviation)				
Left Eye (n = 10, 4)	8.70 (± 36.464)	-4.11 (± 38.380)		
Right Eye (n = 8, 6)	19.05 (± 39.116)	-3.83 (± 21.091)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Reading Accessibility Index of Right Eye and Left Eye at Week 48

End point title	Change From Baseline in Reading Accessibility Index of Right Eye and Left Eye at Week 48

End point description:

Reading Accessibility Index is defined as the mean reading speed in wpm across the 10 largest physical print sizes on the MNREAD Acuity Chart, normalized by the value for a group of normally sighted young adults. For a viewing distance of 40 cm, this range of print sizes corresponds to 0.4 to 1.3 logMAR. Because the Reading Accessibility Index is normalized by the value for a group of normally sighted young adults (aged 18 to 39 years), a Reading Accessibility Index of 1.0 represents normal performance for this age group. Values less than 1.0 mean reduced accessibility to printed text within the range of print size encountered in daily life. Missing data was imputed using LOCF method. The ITT population included all randomized participants who received at least 1 dose of study drug. 'Overall number of participants analyzed' = participants evaluable for this endpoint. 'n' = participants evaluable for specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Ataluren	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	6		
Units: units on a scale				
arithmetic mean (standard deviation)				
Left Eye (n = 11, 4)	-0.70 (± 2.601)	0.01 (± 0.224)		
Right Eye (n = 9, 6)	0.04 (± 0.048)	0.05 (± 0.128)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Critical Print Size (CPS) of Both Eyes, Right Eye, and Left Eye at Week 48

End point title	Change From Baseline in Critical Print Size (CPS) of Both Eyes, Right Eye, and Left Eye at Week 48

End point description:

The MNREAD Acuity Chart test consists of short sentences with print size decreasing by 0.1 log unit steps from a maximum of 1.3 logMAR (equivalent to 20/400 or 6/120 when viewed at 40 cm) to −0.5 logMAR (equivalent to 20/6 or 6/2). An MNREAD Acuity Chart curve of reading speed vs print size has a typical shape for normally sighted persons and many low-vision individuals. This curve is characterized by 3 summary values. At large print sizes, reading speed remains fairly constant, forming a plateau that represents the maximum reading speed. As the print size decreases, a CPS is reached at which reading speed begins to decline rapidly. Finally, the smallest print size that can be read is defined as the RA. Missing data was imputed using LOCF method. The ITT population included all randomized participants who received at least 1 dose of study drug. 'Overall number of participants analyzed' = participants evaluable for this endpoint. 'n' = participants evaluable for specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Ataluren	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	6		
Units: LogMAR				
arithmetic mean (standard deviation)				
Both Eyes (n = 11, 6)	-0.19 (± 0.259)	0.12 (± 0.433)		
Left Eye (n = 10, 4)	-0.05 (± 0.198)	0.07 (± 0.271)		
Right Eye (n = 9, 6)	0.03 (± 0.275)	-0.02 (± 0.452)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Reading Acuity (RA) of Both Eyes, Right Eye, and Left Eye at Week 48

End point title	Change From Baseline in Reading Acuity (RA) of Both Eyes, Right Eye, and Left Eye at Week 48

End point description:

The MNREAD Acuity Chart test consists of short sentences with print size decreasing by 0.1 log unit steps from a maximum of 1.3 logMAR (equivalent to 20/400 or 6/120 when viewed at 40 cm) to −0.5 logMAR (equivalent to 20/6 or 6/2). An MNREAD Acuity Chart curve of reading speed vs print size has a typical shape for normally sighted persons and many low-vision individuals. This curve is characterized by 3 summary values. At large print sizes, reading speed remains fairly constant, forming a plateau that represents the maximum reading speed. As the print size decreases, a CPS is reached at which reading speed begins to decline rapidly. Finally, the smallest print size that can be read is defined as the RA. Missing data was imputed using LOCF method. The ITT population included all randomized participants who received at least 1 dose of study drug. 'Overall number of participants analyzed' = participants evaluable for this endpoint. 'n' = participants evaluable for specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Ataluren	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	6		
Units: LogMAR				
arithmetic mean (standard deviation)				
Both Eyes (n = 11, 6)	-0.06 (± 0.239)	-0.16 (± 0.339)		
Left Eye (n = 11, 4)	-0.15 (± 2.723)	-0.16 (± 0.467)		

Right Eye (n = 9, 6)	-0.05 (± 0.142)	-0.14 (± 0.236)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants With Change From Baseline in Severity of Corneal Keratopathy at Week 48

End point title	Number of participants With Change From Baseline in Severity of Corneal Keratopathy at Week 48

End point description:

The severity of corneal keratopathy was reported as worsened, not change, or improve. Missing data were imputed using LOCF. The ITT population included all randomized participants who received at least 1 dose of study drug. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint. 'n' = participants evaluable for specified category.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	Ataluren	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	12		
Units: participants				
Left Eye: Worsened (n = 19, 7)	4	2		
Left Eye: Not change (n = 19, 7)	7	2		
Left Eye: Improved (n = 19, 7)	8	3		
Right Eye: Worsened (n = 21, 8)	4	2		
Right Eye: Not change (n = 21, 8)	7	2		
Right Eye: Improved (n = 21, 8)	10	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Iris Area at Week 48

End point title	Change From Baseline in Iris Area at Week 48

End point description:

Missing data were imputed using LOCF. The ITT population included all randomized participants who received at least 1 dose of study drug. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint. 'n' = participants evaluable for specified category. '99999' = Dispersion value cannot be calculated for single participant.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Ataluren	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	2		
Units: millimeter square (mm^2)				
arithmetic mean (standard deviation)				
Left Eye (n = 6, 2)	-0.15 (± 0.333)	0.14 (± 0.129)		
Right Eye (n = 9, 1)	-0.06 (± 0.257)	-0.14 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in BCVA at Week 240

End point title	Change From Baseline in BCVA at Week 240

End point description:

The BCVA was evaluated using the ETDRS Method. Missing data were imputed using LOCF method. The ITT population included all randomized participants who received at least 1 dose of study drug. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 240

End point values	Ataluren	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	0[2]		
Units: logMAR				
arithmetic mean (standard deviation)				
Left Eye	0.02 (± 0.141)	()		
Right Eye	0.11 (± 0.240)	()		

Notes:

[2] - None of the participants were evaluable in this arm.

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs)

End point description:

An adverse event (AE) was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. AEs included both SAEs and non-serious AEs. A summary of other non-serious AEs and all SAEs, regardless of causality is located in the 'Reported AE section'. AEs were summarized separately for Stage 1 and for the overall ataluren experience, which included all participants who received ataluren throughput the study (Stage 1, open-label extension period [Stage 2], and sub-study). The safety population included all randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline up to Week 244

End point values	Stage 1: Ataluren	Stage 1: Placebo	Overall Ataluren Exposure	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	26	13	37	
Units: participants	22	10	35	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 244

Adverse event reporting additional description:

The safety population included all randomized participants who received at least 1 dose of study drug. AEs were summarized separately for Stage 1 and for the overall ataluren experience, which included all participants who received ataluren throughput the study (Stage 1, open-label extension period [Stage 2], and sub-study).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Stage 1: Ataluren

Reporting group description:

Participants received ataluren orally TID at a dose of 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for 48 weeks in Stage 1 (double-masked period).

Reporting group title	Stage 1: Placebo

Reporting group description:

Participants received placebo matched to ataluren TID orally in the morning, at midday, and in the evening for 48 weeks in Stage 1 (double-masked period).

Reporting group title	Overall Ataluren Exposure

Reporting group description:

Participants received ataluren orally TID at a dose of 10 mg/kg in the morning, 10 mg/kg at midday, and 20 mg/kg in the evening for 48 weeks in Stage 1 (double-masked period) and for additional 96 weeks in Stage 2 (open-label extension period). Participants, who completed Stage 2 and agreed to continue in open-label sub-study, continued to receive ataluren treatment at same dose as mentioned above, for 96 weeks.

Serious adverse events	Stage 1: Ataluren	Stage 1: Placebo	Overall Ataluren Exposure
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Psychiatric disorders			
Mental disorder			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Stage 1: Ataluren	Stage 1: Placebo	Overall Ataluren Exposure
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 26 (84.62%)	10 / 13 (76.92%)	35 / 37 (94.59%)
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	5 / 26 (19.23%)	2 / 13 (15.38%)	9 / 37 (24.32%)
occurrences (all)	9	3	17
Fatigue			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Local swelling			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Medical device site reaction			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Pyrexia			
subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	6 / 37 (16.22%)
occurrences (all)	2	3	13
Asthenia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Sensation of pressure			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	2
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 37 (0.00%)
occurrences (all)	0	1	0

Balanoposthitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Metrorrhagia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	1 / 37 (2.70%)
occurrences (all)	0	1	2
Epistaxis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	3
Oropharyngeal pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Rhinorrhoea			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Sneezing			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Throat irritation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Mood altered			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Anxiety			

subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Attention deficit/Hyperactivity disorder			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Depression			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Obsessive-compulsive disorder			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	2
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	2 / 37 (5.41%)
occurrences (all)	1	0	2
Urine leukocyte esterase positive			
subjects affected / exposed	2 / 26 (7.69%)	0 / 13 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	3
Blood uric acid increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	2 / 37 (5.41%)
occurrences (all)	1	0	2
Protein urine present			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Nitrite urine present			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Urine ketone body present			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Blood urea increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Intraocular pressure increased			

subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	4
Bacterial test positive			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Blood bilirubin increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Hepatic enzyme increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Concussion			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Corneal Abrasion			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Joint dislocation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Ligament sprain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Radius fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Sunburn			

subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Congenital, familial and genetic disorders			
Phimosis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Nervous system disorders			
Somnolence			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Headache			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	3 / 37 (8.11%)
occurrences (all)	0	1	8
Migraine			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	4
Ear and labyrinth disorders			
Motion sickness			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Eye disorders			
Dry eye			
subjects affected / exposed	4 / 26 (15.38%)	3 / 13 (23.08%)	9 / 37 (24.32%)
occurrences (all)	8	5	24
Lacrimation increased			
subjects affected / exposed	3 / 26 (11.54%)	1 / 13 (7.69%)	10 / 37 (27.03%)
occurrences (all)	6	2	20
Eye pruritus			
subjects affected / exposed	2 / 26 (7.69%)	2 / 13 (15.38%)	13 / 37 (35.14%)
occurrences (all)	4	4	38
Corneal opacity			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	2	0	2
Eye swelling			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	2	0	2

Eyelid ptosis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Lenticular opacities			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	2	0	2
Ocular hyperaemia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	2 / 37 (5.41%)
occurrences (all)	2	0	4
Eye discharge			
subjects affected / exposed	0 / 26 (0.00%)	2 / 13 (15.38%)	3 / 37 (8.11%)
occurrences (all)	0	2	6
Keratopathy			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	1 / 37 (2.70%)
occurrences (all)	0	1	2
Vision blurred			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	1 / 37 (2.70%)
occurrences (all)	0	2	5
Vitreous detachment			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Photophobia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	17 / 37 (45.95%)
occurrences (all)	0	0	38
Eye pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	4 / 37 (10.81%)
occurrences (all)	0	0	8
Lens discolouration			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	4
Blepharospasm			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Cataract			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1

Eye inflammation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	2
Eye irritation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	12
Punctate keratitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Photokeratitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	2
Visual acuity reduced			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	5 / 26 (19.23%)	3 / 13 (23.08%)	9 / 37 (24.32%)
occurrences (all)	6	5	25
Vomiting			
subjects affected / exposed	5 / 26 (19.23%)	3 / 13 (23.08%)	8 / 37 (21.62%)
occurrences (all)	10	5	18
Nausea			
subjects affected / exposed	4 / 26 (15.38%)	2 / 13 (15.38%)	4 / 37 (10.81%)
occurrences (all)	4	2	4
Flatulence			
subjects affected / exposed	3 / 26 (11.54%)	1 / 13 (7.69%)	3 / 37 (8.11%)
occurrences (all)	3	1	3
Abdominal distension			
subjects affected / exposed	2 / 26 (7.69%)	1 / 13 (7.69%)	2 / 37 (5.41%)
occurrences (all)	3	1	3
Frequent bowel movements			
subjects affected / exposed	2 / 26 (7.69%)	0 / 13 (0.00%)	2 / 37 (5.41%)
occurrences (all)	2	0	2
Abdominal pain			

subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	2 / 37 (5.41%)
occurrences (all)	2	0	3
Dental caries			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Diarrhoea			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	2 / 37 (5.41%)
occurrences (all)	1	0	3
Faeces soft			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Tooth impacted			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Abdominal discomfort			
subjects affected / exposed	0 / 26 (0.00%)	2 / 13 (15.38%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Constipation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Gastrointestinal Pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 26 (7.69%)	0 / 13 (0.00%)	2 / 37 (5.41%)
occurrences (all)	2	0	2
Erythema			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Pruritus			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Dermatitis contact			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1

Skin discolouration			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Dysuria			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Epiphysiolysis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	2 / 26 (7.69%)	0 / 13 (0.00%)	7 / 37 (18.92%)
occurrences (all)	2	0	8
Conjunctivitis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	5 / 37 (13.51%)
occurrences (all)	1	0	7
Influenza			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	6 / 37 (16.22%)
occurrences (all)	1	0	7
Nasopharyngitis			
subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	1 / 37 (2.70%)
occurrences (all)	1	1	1
Pharyngitis streptococcal			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	2 / 37 (5.41%)
occurrences (all)	3	0	4
Upper respiratory tract infection			

subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Roseola			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Ear infection			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Atypical Pneumonia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Cellulitis of male external genital organ			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Eye infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	2
Lyme disease			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 February 2016	Increased the frequency of renal monitoring in the study as requested by the Food and Drug Administration (FDA).
13 October 2016	Removed the interim analysis based on the comments from the FDA to SAP V1.0.
20 November 2017	Increased the study period by 48 weeks, for a total study duration of 144 weeks.
17 April 2018	Changed the timing of the primary analysis from Week 48 to Week 96 and provide clarification on the length of the screening period.
08 November 2018	Added a sub-study to include eligible participants who have completed the 144-week parent study to receive an additional 96 weeks of open-label ataluren in order to investigate the safety and efficacy of long-term use.
17 December 2019	Changed the primary endpoint from safety to efficacy in order to investigate the clinical utility of intervention with ataluren in this study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported