Clinical trial results:
Multicenter, Open-Label, Single-Arm Study to Evaluate Long-Term Safety, Tolerability, and Effectiveness of 10 mg/kg BID Olesoxime in Patients With Spinal Muscular Atrophy

Summary

EudraCT number	2015-001589-25
Trial protocol	GB IT DE BE NL FR PL
Global end of trial date	18 December 2018

Results information

Result version number	v1 (current)
This version publication date	22 June 2019
First version publication date	22 June 2019

Trial information

Trial identification

Sponsor protocol code	BN29854

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02628743
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.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	01 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 December 2018
Global end of trial reached?	Yes
Global end of trial date	18 December 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this open-label, single arm study is to further characterize the safety, tolerability and effectiveness profile of olesoxime in Spinal Muscular Atrophy (SMA).

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 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	France: 28
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Italy: 39
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Poland: 20
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	Belgium: 14
Worldwide total number of subjects	131
EEA total number of subjects	131

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)	56
Adolescents (12-17 years)	36

Adults (18-64 years)	39
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 131 patients 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	Olesoxime

Arm description:

Participants received a dose of 10 mg/kg suspension once a day (QD) orally or via a naso-gastric or gastronomy tube. Participants who consented to dose increase received 10 milligrams per kilogram (mg/kg) suspension twice a day (BID) either orally or via a naso-gastric or gastrostomy tube.

Arm type	Experimental
Investigational medicinal product name	Olesoxime
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for oral suspension
Routes of administration	Nasogastric use , Oral use, Gastroenteral use

Dosage and administration details:

Participant will receive 10 milligrams per kilogram (mg/kg) suspension once a day orally or via a naso-gastric or gastronomy tube. Participants who had consented to the dose increase also received 10 mg/kg suspension twice a day (BID).

Number of subjects in period 1	Olesoxime
Started	131
Completed	0
Not completed	131
Consent withdrawn by subject	50
Not Available	3
Physician decision	2
Study Terminated by Sponsor	76

Baseline characteristics

Reporting groups	
Reporting group title	Olesoxime
Reporting group description:	
Participants received a dose of 10 mg/kg suspension once a day (QD) orally or via a naso-gastric or gastronomy tube. Participants who consented to dose increase received 10 milligrams per kilogram (mg/kg) suspension twice a day (BID) either orally or via a naso-gastric or gastrostomy tube.	

Reporting group values	Olesoxime	Total	
Number of subjects	131	131	
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)	56	56	
Adolescents (12-17 years)	36	36	
Adults (18-64 years)	39	39	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	14.7		
standard deviation	± 5.9	-	
Sex: Female, Male Units: Subjects			
Female	66	66	
Male	65	65	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	3	3	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	1	
White	94	94	
More than one race	0	0	
Unknown or Not Reported	33	33	
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	1	1	
Not Hispanic or Latino	89	89	
Not Stated	29	29	
Unknown	12	12	

End points

End points reporting groups

Reporting group title	Olesoxime

Reporting group description:

Participants received a dose of 10 mg/kg suspension once a day (QD) orally or via a naso-gastric or gastronomy tube. Participants who consented to dose increase received 10 milligrams per kilogram (mg/kg) suspension twice a day (BID) either orally or via a naso-gastric or gastrostomy tube.

Primary: Percentage of Participants With Adverse Events (AEs) or Serious Adverse Events (SAEs)

End point title	Percentage of Participants With Adverse Events (AEs) or Serious Adverse Events (SAEs)[1]

End point description:

End point type	Primary

End point timeframe:

Baseline up to approximately 3 years

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: No statistical analyses were defined for this endpoint.

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: percentage of participants				
number (not applicable)				
SAEs	27.5			
AEs	91.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Motor Function Measure (MFM) Dimension 1 (D1) + Dimension 2 (D2) Score

End point title	Change From Baseline in Motor Function Measure (MFM) Dimension 1 (D1) + Dimension 2 (D2) Score

End point description:

The MFM scale evaluated motor function in three dimensions. D1 evaluates functions related to standing and transfer, D2 evaluates axial and proximal function in supine and sitting position on mat and chair and D3 evaluates distal motor function. The scoring of each task uses a 4-point Likert scale based on the participant's maximal abilities without assistance: 0, cannot initiate the task or maintain the starting position; 1, performs the task partially; 2, performs the task incompletely or imperfectly (with compensatory/uncontrolled movements or slowness); and 3, performs the task fully and "normally". The score is expressed as a percentage of the maximum possible score. The lower the total score, the more severe the impairment.

End point type	Secondary

End point timeframe:

Baseline (Week 1), Weeks 26, 52, 78, 104 and 130

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=127)	30.01 (± 12.77)			
Week 26 (n=127)	-0.06 (± 4.75)			
Week 52 (n=111)	-0.31 (± 4.61)			
Week 78 (n=112)	-1.26 (± 5.64)			
Week 104 (n=99)	-3.32 (± 7.08)			
Week 130 (n=64)	-4.87 (± 9.91)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in MFM Total Score (D1+ D2 + Dimension 3 [D3]) Score

End point title	Change From Baseline in MFM Total Score (D1+ D2 + Dimension 3 [D3]) Score

End point description:

The MFM scale evaluated motor function in three dimensions. D1 evaluates functions related to standing and transfer, D2 evaluates axial and proximal function in supine and sitting position on mat and chair and D3 evaluates distal motor function. The scoring of each task uses a 4-point Likert scale based on the participant's maximal abilities without assistance: 0, cannot initiate the task or maintain the starting position; 1, performs the task partially; 2, performs the task incompletely or imperfectly (with compensatory/uncontrolled movements or slowness); and 3, performs the task fully and "normally". The score is expressed as a percentage of the maximum possible score. The lower the total score, the more severe the impairment.

End point type	Secondary

End point timeframe:

Baseline (Week 1), Weeks 26, 52, 78, 104 and 130

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=127)	41.21 (± 12.81)			
Week 26 (n=127)	0.31 (± 4.35)			
Week 52 (n=111)	0.08 (± 4.08)			

Week 78 (n=112)	-0.64 (± 5.28)			
Week 104 (n=99)	-2.96 (± 7.09)			
Week 130 (n=64)	-4.02 (± 9.48)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Olesoxime

End point title	Plasma Concentrations of Olesoxime

End point description:

Values are reported separately for QD and BID doses. Dose increase occurred after Week 104.

End point type	Secondary

End point timeframe:

Pre-dose (Hour 0) at Weeks 1, 13, 26, 39, 52, 78, 104 and 130

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: ng/mL				
arithmetic mean (standard deviation)				
Baseline (n=128)	129.0 (± 160.2)			
Week 13 (n=128)	9475.5 (± 3962.5)			
Week 26 (n=119)	10021.3 (± 4885.6)			
Week 39 (n=117)	10257.8 (± 4443.7)			
Week 52 (n=112)	9665.6 (± 4941.8)			
Week 78 (n=107)	10351.4 (± 5267.3)			
Week 104 (n=100)	8566.4 (± 5353.1)			
Dose Increase Visit (BID) (n=19)	14797.1 (± 5773.8)			
Week 130 (QD) (n=46)	6274.6 (± 6281.9)			
Week 130 (BID) (n=20)	13956.9 (± 9565.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pediatric Quality of Life Questionnaire (PedsQL)

Generic Core Scale Version 4.0 Score

End point title	Change from Baseline in Pediatric Quality of Life Questionnaire (PedsQL) Generic Core Scale Version 4.0 Score

End point description:

The PedsQL Generic Core Scale includes 23 items using self-report and/or parent report (ages 5+). The instrument covers physical, emotional, social and school functioning. Scale items are linearly transformed to a 0–100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, and 4 = 0) so that higher scores indicate better health related quality of life.

End point type	Secondary

End point timeframe:

Baseline (Week 1), Weeks 26, 52, 78, 104 and 130

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (Total Score) (n=128)	58.69 (± 11.17)			
Total Score - Week 26 (n=126)	-0.80 (± 9.10)			
Total Score - Week 52 (n=118)	-1.33 (± 10.52)			
Total Score - Week 78 (n=109)	-0.72 (± 10.98)			
Total Score - Week 104 (n=101)	-0.35 (± 11.69)			
Total Score - Week 130 (n=67)	-0.11 (± 10.83)			
Baseline (Physical Score) (n=128)	28.49 (± 16.50)			
Physical Score - Week 26 (n=126)	-1.76 (± 15.99)			
Physical Score - Week 52 (n=117)	-4.48 (± 17.68)			
Physical Score - Week 78 (n=109)	-3.18 (± 19.67)			
Physical Score - Week 104 (n=101)	-1.42 (± 17.87)			
Physical Score - Week 130 (n=67)	-3.23 (± 16.33)			
Baseline (Emotional Score) (n=128)	74.61 (± 17.34)			
Emotional Score - Week 26 (n=126)	-1.19 (± 18.62)			
Emotional Score - Week 52 (n=118)	1.19 (± 16.27)			
Emotional Score - Week 78 (n=108)	-0.05 (± 17.23)			
Emotional Score - Week 104 (n=101)	-0.54 (± 18.37)			
Emotional Score - Week 130 (n=67)	2.31 (± 18.47)			
Baseline (Social Score) (n=128)	72.77 (± 18.59)			
Social Score - Week 26 (n=126)	1.43 (± 14.15)			
Social Score - Week 52 (n=118)	0.93 (± 15.91)			
Social Score - Week 78 (n=109)	2.39 (± 17.38)			

Social Score - Week 104 (n=101)	2.38 (± 18.62)			
Social Score - Week 130 (n=67)	4.10 (± 16.05)			
Baseline (School/Work Score) (n=127)	77.20 (± 15.83)			
School/Work Score - Week 26 (n=125)	-1.24 (± 14.28)			
School/Work Score - Week 52 (n=117)	-1.32 (± 14.09)			
School/Work Score - Week 78 (n=107)	-0.51 (± 14.26)			
School/Work Score - Week 104 (n=100)	-1.65 (± 15.24)			
School/Work Score - Week 130 (n=66)	-2.58 (± 15.04)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Caregiver PedsQL Generic Core Scales Version 4.0 Score

End point title	Change from Baseline in Caregiver PedsQL Generic Core Scales Version 4.0 Score

End point description:

The PedsQL Generic Core Scale includes 23 items. The instrument covers physical, emotional, social and school functioning. Scale items are linearly transformed to a 0–100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, and 4 = 0) so that higher scores indicate better health related quality of life. Questionnaire was completed by the caregiver.

End point type	Secondary

End point timeframe:

Baseline (Week 1), Weeks 26, 52, 78, 104 and 130

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (Total Score) (n=121)	55.58 (± 12.49)			
Total Score - Week 26 (n=115)	-0.85 (± 13.15)			
Total Score - Week 52 (n=106)	-1.86 (± 13.12)			
Total Score - Week 78 (n=103)	-0.67 (± 13.88)			
Total Score - Week 104 (n=93)	-1.64 (± 17.95)			
Total Score - Week 130 (n=62)	-0.33 (± 13.41)			
Baseline (Physical Score) (n=121)	28.99 (± 25.84)			

Physical Score - Week 26 (n=115)	-0.58 (± 28.66)			
Physical Score - Week 52 (n=106)	-5.10 (± 25.86)			
Physical Score - Week 78 (n=103)	-2.91 (± 28.91)			
Physical Score - Week 104 (n=93)	-3.28 (± 34.80)			
Physical Score - Week 130 (n=62)	-0.56 (± 30.09)			
Baseline (Emotional Score) (n=121)	67.48 (± 17.31)			
Emotional Score - Week 26 (n=115)	-2.13 (± 15.30)			
Emotional Score - Week 52 (n=106)	-0.90 (± 15.08)			
Emotional Score - Week 78 (n=103)	-0.39 (± 18.81)			
Emotional Score - Week 104 (n=93)	-0.70 (± 20.54)			
Emotional Score - Week 130 (n=62)	-0.32 (± 15.94)			
Baseline (Social Score) (n=121)	68.34 (± 16.19)			
Social Score - Week 26 (n=115)	-0.42 (± 16.84)			
Social Score - Week 52 (n=106)	-0.49 (± 15.92)			
Social Score - Week 78 (n=103)	1.47 (± 18.40)			
Social Score - Week 104 (n=93)	-0.55 (± 21.72)			
Social Score - Week 130 (n=61)	1.25 (± 16.22)			
Baseline (School/Work Score) (n=120)	73.67 (± 17.69)			
School/Work Score - Week 26 (n=112)	-0.31 (± 16.69)			
School/Work Score - Week 52 (n=104)	0.53 (± 18.14)			
School/Work Score - Week 78 (n=101)	0.94 (± 18.39)			
School/Work Score - Week 104 (n=91)	-0.71 (± 20.64)			
School/Work Score - Week 130 (n=59)	-1.53 (± 16.17)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in PedsQL Neuromuscular Module Version 3.0 Scale Score

End point title	Change from Baseline in PedsQL Neuromuscular Module Version 3.0 Scale Score

End point description:

The PedsQL Neuromuscular Module (Version 3.0) includes 25 items using self-report (ages 5 - 18) and/or parent report (ages 5 -18). The instrument covers problems related to neuromuscular disease, communication and family resources. Scale items are linearly transformed to a 0–100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, and 4 = 0) so that higher scores indicate better health related quality of life.

End point type	Secondary

End point timeframe:
Baseline (Week 1), Weeks 26, 52, 78, 104 and 130

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (Total Score) (n=90)	69.57 (± 14.01)			
Total Score - Week 26 (n=89)	-0.98 (± 10.75)			
Total Score - Week 52 (n=81)	-0.86 (± 12.81)			
Total Score - Week 78 (n=79)	-1.08 (± 12.11)			
Total Score - Week 104 (n=70)	-1.18 (± 13.13)			
Total Score - Week 130 (n=52)	-1.41 (± 12.61)			
Baseline (Neuromuscular) (n=90)	66.03 (± 15.39)			
Neuromuscular - Week 26 (n=89)	-1.77 (± 12.28)			
Neuromuscular - Week 52 (n=81)	-2.22 (± 14.29)			
Neuromuscular - Week 78 (n=79)	-2.69 (± 12.82)			
Neuromuscular - Week 104 (n=70)	-1.90 (± 15.11)			
Neuromuscular - Week 130 (n=52)	-3.14 (± 14.20)			
Baseline (Family Resources Score) (n=90)	74.39 (± 20.10)			
Family Resources Score - Week 26 (n=89)	-0.11 (± 17.35)			
Family Resources Score - Week 52 (n=80)	1.78 (± 16.07)			
Family Resources Score - Week 78 (n=79)	0.82 (± 19.22)			
Family Resources Score - Week 104 (n=70)	-1.29 (± 19.81)			
Family Resources Score - Week 130 (n=52)	-0.38 (± 16.36)			
Baseline (Communication Score) (n=90)	81.57 (± 21.14)			
Communication Score - Week 26 (n=89)	2.01 (± 19.86)			
Communication Score - Week 52 (n=81)	1.44 (± 24.43)			
Communication Score - Week 78 (n=79)	4.85 (± 22.19)			
Communication Score - Week 104 (n=70)	2.98 (± 24.25)			
Communication Score - Week 130 (n=52)	6.57 (± 25.15)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Caregiver PedsQL Neuromuscular Module Version 3.0 Scale Score

End point title	Change from Baseline in Caregiver PedsQL Neuromuscular Module Version 3.0 Scale Score

End point description:

The PedsQL Neuromuscular Module (Version 3.0) includes 25 items using self-report (ages 5 - 18) and/or parent report (ages 5 -18). The instrument covers problems related to neuromuscular disease, communication and family resources. Scale items are linearly transformed to a 0–100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, and 4 = 0) so that higher scores indicate better health related quality of life. Questionnaire was completed by the caregiver.

End point type	Secondary

End point timeframe:

Baseline (Week 1), Weeks 26, 52, 78, 104 and 130

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (Total Score) (n=88)	59.44 (± 14.83)			
Total Score - Week 26 (n=87)	0.13 (± 10.12)			
Total Score - Week 52 (n=78)	-0.11 (± 12.89)			
Total Score - Week 78 (n=77)	0.65 (± 13.23)			
Total Score - Week 104 (n=67)	1.21 (± 14.40)			
Total Score - Week 130 (n=51)	-0.07 (± 12.86)			
Baseline (Neuromuscular) (n=88)	56.28 (± 15.70)			
Neuromuscular - Week 26 (n=87)	-0.64 (± 10.92)			
Neuromuscular - Week 52 (n=78)	-1.33 (± 13.39)			
Neuromuscular - Week 78 (n=77)	0.05 (± 13.97)			
Neuromuscular - Week 104 (n=67)	0.54 (± 15.32)			
Neuromuscular - Week 130 (n=51)	-1.39 (± 14.65)			
Baseline (Family Resources Score) (n=88)	58.24 (± 25.08)			
Family Resources Score - Week 26 (n=86)	1.74 (± 16.57)			

Family Resources Score - Week 52 (n=77)	2.44 (± 19.04)			
Family Resources Score - Week 78 (n=77)	0.91 (± 19.31)			
Family Resources Score - Week 104 (n=67)	1.27 (± 18.63)			
Family Resources Score - Week 130 (n=50)	1.00 (± 17.26)			
Baseline (Communication Score) (n=88)	79.36 (± 22.92)			
Communication Score - Week 26 (n=87)	1.92 (± 20.08)			
Communication Score - Week 52 (n=78)	2.88 (± 22.31)			
Communication Score - Week 78 (n=77)	3.57 (± 20.92)			
Communication Score - Week 104 (n=67)	4.85 (± 24.24)			
Communication Score - Week 130 (n=51)	4.90 (± 22.74)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in EuroQol 5-Dimension 5-Level (EQ-5D-5L) Questionnaire Index Score - Total Score

End point title	Change from Baseline in EuroQol 5-Dimension 5-Level (EQ-5D-5L) Questionnaire Index Score - Total Score

End point description:

The EQ-5D-5L is a self-reported health status questionnaire that consists of six questions used to calculate a health utility score for use in health economic analysis. There are two components to the EQ-5D-5L: a five-item health state profile that assesses mobility, self-care, usual activities, pain/discomfort, and anxiety/depression used to obtain an Index Utility Score, as well as a visual analogue scale (VAS) that measures health state. Overall scores range from 0 to 1, with low scores representing a higher level of dysfunction.

End point type	Secondary

End point timeframe:

Baseline (Week 1), Weeks 26, 52, 78, 104, 130; thereafter every 26 weeks up to 5 years

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=74)	0.0471 (± 0.1345)			
Week 26 (n=72)	0.0084 (± 0.1563)			
Week 52 (n=68)	-0.0164 (± 0.1191)			
Week 78 (n=66)	0.0168 (± 0.1910)			
Week 104 (n=57)	0.0081 (± 0.1701)			

Week 130 (n=34)	-0.0259 (± 0.1232)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Caregiver Proxy EQ-5D-5L Questionnaire Index Score - Total Score

End point title	Change from Baseline in Caregiver Proxy EQ-5D-5L Questionnaire Index Score - Total Score

End point description:

The EQ-5D-5L is a self-reported health status questionnaire that consists of six questions used to calculate a health utility score for use in health economic analysis. There are two components to the EQ-5D-5L: a five-item health state profile that assesses mobility, self-care, usual activities, pain/discomfort, and anxiety/depression used to obtain an Index Utility Score, as well as a visual analogue scale (VAS) that measures health state. Overall scores range from 0 to 1, with low scores representing a higher level of dysfunction. The questionnaire was completed by the caregiver.

End point type	Secondary

End point timeframe:

Baseline (Week 1), Weeks 26, 52, 78, 104, 130; thereafter every 26 weeks up to 5 years

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=54)	0.0429 (± 0.2335)			
Week 26 (n=50)	0.0652 (± 0.4091)			
Week 52 (n=47)	0.0203 (± 0.2820)			
Week 78 (n=47)	0.0696 (± 0.3094)			
Week 104 (n=39)	0.0699 (± 0.2887)			
Week 130 (n=31)	0.0455 (± 0.3323)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in EQ-5D-5L Visual Analogue Scale (EQ-5D-5L VAS) Score

End point title	Change from Baseline in EQ-5D-5L Visual Analogue Scale (EQ-5D-5L VAS) Score

End point description:

The EQ-5D-5L is a self-reported health status questionnaire that consists of six questions used to calculate a health utility score for use in health economic analysis. There are two components to the EQ-5D-5L: a five-item health state profile that assesses mobility, self-care, usual activities, pain/discomfort, and anxiety/depression used to obtain an Index Utility Score, as well as a visual analogue scale (VAS) that measures health state. The VAS is designed to rate the participant's current health state on a scale from 0 to 100, where 0 represents the worst imaginable health state and 100 represents the best imaginable health state.

End point type	Secondary

End point timeframe:

Baseline (Week 1), Weeks 26, 52, 78, 104, 130; thereafter every 26 weeks up to 5 years

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=75)	69.4 (± 19.7)			
Week 26 (n=73)	1.3 (± 17.1)			
Week 52 (n=69)	0.2 (± 17.4)			
Week 78 (n=67)	1.3 (± 19.9)			
Week 104 (n=58)	5.4 (± 17.0)			
Week 130 (n=35)	0.6 (± 18.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Caregiver Proxy EQ-5D-5L VAS Score

End point title	Change from Baseline in Caregiver Proxy EQ-5D-5L VAS Score

End point description:

The EQ-5D-5L is a self-reported health status questionnaire that consists of six questions used to calculate a health utility score for use in health economic analysis. There are two components to the EQ-5D-5L: a five-item health state profile that assesses mobility, self-care, usual activities, pain/discomfort, and anxiety/depression used to obtain an Index Utility Score, as well as a visual analogue scale (VAS) that measures health state. The VAS is designed to rate the participant's current health state on a scale from 0 to 100, where 0 represents the worst imaginable health state and 100 represents the best imaginable health state. Questionnaire was completed by the caregiver.

End point type	Secondary

End point timeframe:

Baseline (Week 1), Weeks 26, 52, 78, 104, 130; thereafter every 26 weeks up to 5 years

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=54)	72.7 (± 21.4)			
Week 26 (n=49)	-0.3 (± 27.7)			
Week 52 (n=47)	0.8 (± 21.2)			
Week 78 (n=47)	0.4 (± 20.9)			
Week 104 (n=40)	5.7 (± 24.3)			
Week 130 (n=31)	0.5 (± 17.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Employed Assessed Using the Work Productivity and Activity Impairment Questionnaire: Caregiver (WPAI:CG) Questionnaire

End point title	Number of Subjects Employed Assessed Using the Work Productivity and Activity Impairment Questionnaire: Caregiver (WPAI:CG) Questionnaire

End point description:

The WPAI:CG consists of four questions about the effects of Spinal Muscular Atrophy (SMA) on the following: employment status, hours missed due to patient caregiving, hours missed due to other reasons, hours actually worked and two questions that measure the degree to which patient caregiving affected productivity and regular daily activities.

End point type	Secondary

End point timeframe:

Baseline (Week 1), Weeks 26, 52, 78, 104 and 130

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: participants				
Baseline (n=121)	56			
Week 26 (n=119)	66			
Week 52 (n=109)	58			
Week 78 (n=107)	62			
Week 104 (n=97)	56			
Week 130 (n=65)	39			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Hours Actually Worked and Work Hours Missed Assessed Using WPAI:CG Questionnaire

End point title	Change from Baseline in Hours Actually Worked and Work Hours Missed Assessed Using WPAI:CG Questionnaire

End point description:

The WPAI:CG consists of four questions about the effects of SMA on the following: employment status, hours missed due to patient caregiving (HMC), hours missed due to other reasons (HMO), hours actually worked (HAW) and two questions that measure the degree to which patient caregiving affected productivity and regular daily activities.

End point type	Secondary

End point timeframe:

Baseline (Week 1), Weeks 26, 52, 78, 104 and 130

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: hours				
arithmetic mean (standard deviation)				
Baseline (HMC) (n=56)	2.0 (± 3.7)			
HMC, Week 26 (n=50)	2.0 (± 7.3)			
HMC, Week 52 (n=44)	1.9 (± 8.2)			
HMC, Week 78 (n=49)	0.9 (± 5.6)			
HMC, Week 104 (n=45)	3.2 (± 8.3)			
HMC, Week 130 (n=35)	1.1 (± 8.1)			
Baseline (HMO) (n=56)	4.8 (± 7.3)			
HMO, Week 26 (n=51)	-1.5 (± 7.9)			
HMO, Week 52 (n=43)	-1.5 (± 9.0)			
HMO, Week 78 (n=49)	-0.1 (± 8.6)			
HMO, Week 104 (n=45)	0.0 (± 9.6)			
HMO, Week 130 (n=35)	0.8 (± 7.8)			
Baseline (HAW) (n=56)	36.0 (± 47.0)			
HAW, Week 26 (n=51)	-12.0 (± 46.7)			
HAW, Week 52 (n=43)	-8.3 (± 49.2)			
HAW, Week 78 (n=48)	-8.6 (± 49.8)			
HAW, Week 104 (n=44)	1.2 (± 14.4)			
HAW, Week 130 (n=35)	1.5 (± 27.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Work Time Missed, Impairment While Working, Overall Work Impairment and Activity Impairment Assessed Using WPAI:CG Questionnaire Score

End point title	Change from Baseline in Work Time Missed, Impairment While Working, Overall Work Impairment and Activity Impairment Assessed Using WPAI:CG Questionnaire Score

End point description:

The WPAI:CG consists of four questions about the effects of Spinal Muscular Atrophy (SMA) on the following: employment status, hours missed due to patient caregiving, hours missed due to other reasons, hours actually worked and two questions that measure the degree to which patient caregiving affected productivity and regular daily activities. WPAI:CG outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity. The outcomes are presented for Percent work time missed (WTM), Percent impairment (IMP), Percent overall work impairment (OWI) and Percent activity impairment (AIM).

End point type	Secondary

End point timeframe:

Baseline (Week 1), Weeks 26, 52, 78, 104 and 130

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: percentage				
arithmetic mean (standard deviation)				
Baseline (WTM) (n=53)	6.7 (± 11.9)			
WTM, Week 26 (n=44)	7.0 (± 22.3)			
WTM, Week 52 (n=38)	0.8 (± 15.4)			
WTM, Week 78 (n=43)	6.2 (± 23.3)			
WTM, Week 104 (n=39)	6.7 (± 20.1)			
WTM, Week 130 (n=31)	4.7 (± 24.4)			
Baseline (IMP) (n=56)	29.3 (± 26.6)			
IMP, Week 26 (n=50)	-3.0 (± 22.8)			
IMP, Week 52 (n=46)	-1.5 (± 27.3)			
IMP, Week 78 (n=49)	-3.5 (± 25.0)			
IMP, Week 104 (n=45)	0.7 (± 22.8)			
IMP, Week 130 (n=35)	-6.9 (± 24.7)			
Baseline (OWI) (n=53)	33.8 (± 28.1)			
OWI, Week 26 (n=43)	-3.6 (± 25.3)			
OWI, Week 52 (n=38)	-3.3 (± 25.4)			
OWI, Week 78 (n=43)	-3.0 (± 31.9)			
OWI, Week 104 (n=39)	3.5 (± 26.2)			
OWI, Week 130 (n=31)	-3.4 (± 33.3)			
Baseline (AIM) (n=121)	45.8 (± 29.3)			
AIM, Week 26 (n=114)	-3.9 (± 28.7)			
AIM, Week 52 (n=106)	-1.3 (± 30.6)			
AIM, Week 78 (n=105)	-6.3 (± 32.6)			
AIM, Week 104 (n=94)	-7.6 (± 27.8)			
AIM, Week 130 (n=64)	-5.5 (± 31.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Degree Patient Caregiving Affected Productivity and Activities Using WPAI:CG Questionnaire

End point title	Change from Baseline in Degree Patient Caregiving Affected Productivity and Activities Using WPAI:CG Questionnaire

End point description:

The WPAI:CG consists of four questions about the effects of Spinal Muscular Atrophy (SMA) on the following: employment status, hours missed due to patient caregiving, hours missed due to other reasons, hours actually worked and two questions that measure the degree to which patient caregiving affected productivity and regular daily activities. WPAI:CG outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity.

End point type	Secondary

End point timeframe:

Baseline (Week 1), Weeks 26, 52, 78, 104 and 130

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: percentage				
arithmetic mean (standard deviation)				
Baseline (Productivity) (n=56)	29.3 (± 26.6)			
Productivity, Week 26 (n=50)	-3.0 (± 22.8)			
Productivity, Week 52 (n=46)	-1.5 (± 27.3)			
Productivity, Week 78 (n=49)	-3.5 (± 25.0)			
Productivity, Week 104 (n=45)	0.7 (± 22.8)			
Productivity, Week 130 (n=35)	-6.9 (± 24.7)			
Baseline (Activities) (n=121)	45.8 (± 29.3)			
Activities, Week 26 (n=114)	-3.9 (± 28.7)			
Activities, Week 52 (n=106)	-1.3 (± 30.6)			
Activities, Week 78 (n=105)	-6.3 (± 32.6)			
Activities, Week 104 (n=94)	-7.6 (± 27.8)			
Activities, Week 130 (n=64)	-5.5 (± 31.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Short-Form 36 (SF-36) Physical Composite Scores (PCS) and Mental Composite Scores (MCS): Caregiver

End point title	Change from Baseline in Short-Form 36 (SF-36) Physical Composite Scores (PCS) and Mental Composite Scores (MCS): Caregiver

End point description:

The SF-36 was used to assess health-related quality of life at baseline and at on-treatment visits. The SF-36 consisted of 36 questions covering 8 domains (physical functioning, role-functioning physical, bodily pain, general health, vitality, social functioning, role-functioning emotional and mental health), with each domain scoring on a scale 0-100 (a score of 0 = maximum disability and a score of 100 = no disability). The 8 domains are further summarized to 2 distinct higher-ordered clusters: the physical and mental composite t-scores (PCS and MCS). The range for all 8 domains as well as for the composite norm-based t-scores is from 0 to 100 with 100 as best possible health status and 0 as worst health status. Reported here are the Physical Composite Scores (PCS) and Mental Composite Scores (MCS).

End point type	Secondary

End point timeframe:

Baseline (Week 1), Weeks 26, 52, 78, 104 and 130

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (PCS) (n=99)	48.07 (± 10.33)			
PCS, Week 26 (n=95)	-0.24 (± 10.95)			
PCS, Week 52 (n=87)	0.27 (± 9.73)			
PCS, Week 78 (n=88)	-0.34 (± 10.87)			
PCS, Week 104 (n=77)	-0.48 (± 10.30)			
PCS, Week 130 (n=56)	1.68 (± 12.94)			
Baseline (MCS) (n=101)	49.71 (± 10.52)			
MCS, Week 26 (n=97)	-1.05 (± 10.22)			
MCS, Week 52 (n=89)	-1.64 (± 10.06)			
MCS, Week 78 (n=90)	-0.21 (± 9.30)			
MCS, Week 104 (n=79)	-0.08 (± 7.73)			
MCS, Week 130 (n=57)	-1.21 (± 9.98)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 Domain Scores: Caregiver

End point title	Change from Baseline in SF-36 Domain Scores: Caregiver

End point description:

The SF-36 was used to assess health-related quality of life at baseline and at on-treatment visits. The SF-36 consisted of 36 questions covering 8 domains (physical functioning, role-functioning physical, bodily pain, general health, vitality, social functioning, role-functioning emotional and mental health), with each domain scoring on a scale 0-100 (a score of 0 = maximum disability and a score of 100 = no disability). The range for all 8 norm-based domains was from 0 to 100 with 100 as best possible health status and 0 as worst health status.

End point type	Secondary

End point timeframe:

Baseline (Week 1), Weeks 26, 52, 78, 104 and 130

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (Physical) (n=99)	44.51 (± 15.97)			
Physical, Week 26 (n=95)	1.73 (± 16.36)			
Physical, Week 52 (n=87)	2.03 (± 14.23)			
Physical, Week 78 (n=88)	1.25 (± 16.16)			
Physical, Week 104 (n=77)	2.39 (± 16.61)			
Physical, Week 130 (n=56)	6.02 (± 18.87)			
Baseline (Role (Physical)) (n=101)	47.95 (± 8.83)			
Role (physical), Week 26 (n=97)	-1.18 (± 10.29)			
Role (physical), Week 52 (n=89)	-0.76 (± 9.45)			
Role (physical), Week 78 (n=90)	-1.02 (± 9.82)			
Role (physical), Week 104 (n=79)	-1.05 (± 8.92)			
Role (physical), Week 130 (n=57)	-0.35 (± 10.75)			
Baseline (Bodily pain) (n=101)	50.94 (± 8.77)			
Bodily pain, Week 26 (n=97)	-1.82 (± 8.75)			
Bodily pain, Week 52 (n=89)	-1.83 (± 9.04)			
Bodily pain, Week 78 (n=90)	-2.14 (± 10.55)			
Bodily pain, Week 104 (n=79)	-2.40 (± 8.44)			
Bodily pain, Week 130 (n=57)	-2.96 (± 9.82)			
Baseline (General health) (n=101)	50.21 (± 10.65)			
General health, Week 26 (n=97)	-0.63 (± 10.59)			
General health, Week 52 (n=89)	-0.75 (± 9.64)			
General health, Week 78 (n=90)	-0.22 (± 10.83)			
General health, Week 104 (n=79)	-1.17 (± 11.22)			
General health, Week 130 (n=57)	1.07 (± 11.87)			
Baseline (Vitality) (n=101)	51.28 (± 9.42)			
Vitality, Week 26 (n=97)	-1.04 (± 8.48)			
Vitality, Week 52 (n=89)	-1.23 (± 7.53)			
Vitality, Week 78 (n=90)	-0.03 (± 9.67)			
Vitality, Week 104 (n=79)	-0.07 (± 8.16)			
Vitality, Week 130 (n=57)	0.37 (± 8.57)			
Baseline (Social) (n=101)	48.01 (± 9.49)			
Social, Week 26 (n=97)	-0.67 (± 10.60)			
Social, Week 52 (n=89)	-1.24 (± 11.14)			
Social, Week 78 (n=90)	0.28 (± 10.29)			
Social, Week 104 (n=79)	-0.95 (± 9.12)			
Social, Week 130 (n=57)	0.35 (± 10.46)			
Baseline (Role (emotional)) (n=101)	48.38 (± 9.58)			
Role (emotional), Week 26 (n=97)	-1.15 (± 10.59)			

Role (emotional), Week 52 (n=89)	-1.72 (± 11.38)			
Role (emotional), Week 78 (n=90)	-1.16 (± 10.58)			
Role (emotional), Week 104 (n=79)	-1.06 (± 8.03)			
Role (emotional), Week 130 (n=57)	-0.43 (± 9.87)			
Baseline (Mental health) (n=101)	48.46 (± 9.39)			
Mental health, Week 26 (n=97)	-0.24 (± 9.73)			
Mental health, Week 52 (n=89)	-0.50 (± 9.15)			
Mental health, Week 78 (n=90)	0.07 (± 7.77)			
Mental health, Week 104 (n=79)	1.32 (± 7.42)			
Mental health, Week 130 (n=57)	-0.29 (± 9.21)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Revised Utility Index Score (SF-6D_R2): Caregiver

End point title	Change from Baseline in Revised Utility Index Score (SF-6D_R2): Caregiver

End point description:

The SF-6D focuses on seven of the eight health domains covered by the SF-36: physical functioning, role participation (combined role-physical and role-emotional), social functioning, bodily pain, mental health, and vitality. SF-6D Health Utility Index (HUI) Score = 0 (worst measured health state) to 1 (best measured health state).

End point type	Secondary

End point timeframe:

Baseline (Week 1), Weeks 26, 52, 78, 104 and 130

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=98)	0.70 (± 0.11)			
Week 26 (n=92)	-0.01 (± 0.12)			
Week 52 (n=86)	-0.01 (± 0.10)			
Week 78 (n=87)	-0.01 (± 0.12)			
Week 104 (n=76)	0.00 (± 0.11)			
Week 130 (n=54)	0.01 (± 0.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: SMA Independence Scale (SMAIS) Score: Patient and Caregiver

End point title	SMA Independence Scale (SMAIS) Score: Patient and Caregiver

End point description:

The SMAIS was developed specifically for SMA in order to assess function-related independence. The SMAIS contains 29 items, assessing the amount of assistance required from another individual to perform daily activities, such as eating or transferring to/from a wheelchair. Each item is scored on a zero to four scale (with an additional option to indicate that an item is non-applicable). Item scores are summed to create the total score. Lower scores indicate greater dependence on another individual.

End point type	Secondary

End point timeframe:

Week 104 and Week 130

End point values	Olesoxime			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: score on scale				
arithmetic mean (standard deviation)				
Patient, Week 104 (n=14)	71.7 (± 23.4)			
Patient, Week 130 (n=12)	74.8 (± 22.5)			
Caregiver, Week 104 (n=20)	60.1 (± 22.2)			
Caregiver, Week 130 (n=17)	58.0 (± 24.9)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to approximately 3 years	
Adverse event reporting additional description:	
Safety population included all patients who received at least one dose of study medication.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	Olesoxime
Reporting group description:	
Participants received a dose of 10 mg/kg suspension once a day (QD) orally or via a naso-gastric or gastronomy tube. Participants who consented to dose increase received 10 milligrams per kilogram (mg/kg) suspension twice a day (BID) either orally or via a naso-gastric or gastrostomy tube.	

Serious adverse events	Olesoxime		
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 131 (27.48%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
ACCIDENTAL OVERDOSE			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
FALL			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
FEMORAL NECK FRACTURE			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
FEMUR FRACTURE			

subjects affected / exposed	2 / 131 (1.53%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
HUMERUS FRACTURE				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
JOINT DISLOCATION				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
POSTOPERATIVE WOUND COMPLICATION				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PROCEDURAL HAEMORRHAGE				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PROCEDURAL PAIN				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PROCEDURAL PNEUMOTHORAX				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
THERMAL BURN				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
MEDICAL DEVICE REMOVAL				

subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SKIN GRAFT			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
CONSTIPATION			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
VOMITING			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
GASTRITIS			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
TESTICULAR TORSION			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LUNG DISORDER			

subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
OBSTRUCTIVE AIRWAYS DISORDER			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RESPIRATORY DISTRESS			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
RESPIRATORY FAILURE			
subjects affected / exposed	2 / 131 (1.53%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DEPRESSED MOOD			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
NEPHROLITHIASIS			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

PATHOLOGICAL FRACTURE				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
BRONCHITIS				
subjects affected / exposed	3 / 131 (2.29%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
GASTROENTERITIS				
subjects affected / exposed	2 / 131 (1.53%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
UPPER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	2 / 131 (1.53%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
ENCEPHALITIS				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
GASTROINTESTINAL INFECTION				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
LOWER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	4 / 131 (3.05%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
LUNG INFECTION				
subjects affected / exposed	2 / 131 (1.53%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

OSTEOMYELITIS				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA				
subjects affected / exposed	10 / 131 (7.63%)			
occurrences causally related to treatment / all	0 / 13			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA VIRAL				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
POSTOPERATIVE WOUND INFECTION				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
RESPIRATORY TRACT INFECTION				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
URINARY TRACT INFECTION				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
VIRAL UPPER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
FOOD REFUSAL				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	Olesoxime		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	105 / 131 (80.15%)		
Nervous system disorders			
HEADACHE			
subjects affected / exposed	23 / 131 (17.56%)		
occurrences (all)	44		
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	28 / 131 (21.37%)		
occurrences (all)	40		
Gastrointestinal disorders			
ABDOMINAL PAIN UPPER			
subjects affected / exposed	8 / 131 (6.11%)		
occurrences (all)	12		
CONSTIPATION			
subjects affected / exposed	9 / 131 (6.87%)		
occurrences (all)	13		
DIARRHOEA			
subjects affected / exposed	20 / 131 (15.27%)		
occurrences (all)	34		
NAUSEA			
subjects affected / exposed	9 / 131 (6.87%)		
occurrences (all)	13		
VOMITING			
subjects affected / exposed	23 / 131 (17.56%)		
occurrences (all)	43		
Respiratory, thoracic and mediastinal disorders			
COUGH			

subjects affected / exposed occurrences (all) OROPHARYNGEAL PAIN subjects affected / exposed occurrences (all)	17 / 131 (12.98%) 23 16 / 131 (12.21%) 29		
Skin and subcutaneous tissue disorders RASH subjects affected / exposed occurrences (all)	 8 / 131 (6.11%) 10		
Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all) BACK PAIN subjects affected / exposed occurrences (all) MUSCULOSKELETAL PAIN subjects affected / exposed occurrences (all)	 12 / 131 (9.16%) 14 9 / 131 (6.87%) 16 8 / 131 (6.11%) 8		
Infections and infestations BRONCHITIS subjects affected / exposed occurrences (all) GASTROENTERITIS subjects affected / exposed occurrences (all) INFLUENZA subjects affected / exposed occurrences (all) NASOPHARYNGITIS subjects affected / exposed occurrences (all) PHARYNGITIS subjects affected / exposed occurrences (all) RHINITIS	 15 / 131 (11.45%) 22 13 / 131 (9.92%) 18 13 / 131 (9.92%) 14 30 / 131 (22.90%) 57 7 / 131 (5.34%) 9		

subjects affected / exposed	10 / 131 (7.63%)		
occurrences (all)	15		
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	36 / 131 (27.48%)		
occurrences (all)	63		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 September 2015	Clarity regarding contraception use, as well as withdrawal in case of pregnancy have been included in the protocol.
19 August 2016	The Hammersmith Functional Motor Scale (HFMS) scale was removed to decrease patient and site burden, the use of anticoagulants as prohibited medications was removed to align with the Investigator's Brochure and added new information regarding pharmacokinetic characteristics of the study drug.
14 November 2017	Olesoxime dose increased from 10 mg/kg once daily (QD) to 10 mg/kg twice daily (BID) and a newly developed scale assessing function-related independence has been introduced as a patient-reported outcome measure: the SMA Independence Scale (SMAIS).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported