Clinical trial results:
Protocol TRO19622CLEQ1275-1 (WN29836) Phase II, Multicenter, Randomized, Adaptive, Double-Blind, Placebo Controlled Study to Assess Safety and Efficacy of Olesoxime (TRO19622) in 3-25 Year Old Spinal Muscular Atrophy (SMA) Patients

Summary

EudraCT number	2010-020386-24
Trial protocol	FR NL BE DE IT GB
Global end of trial date	09 October 2013

Results information

Result version number	v1 (current)
This version publication date	25 January 2018
First version publication date	25 January 2018

Trial information

Trial identification

Sponsor protocol code	WN29836

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01302600
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	Medical Communications, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	Medical Communications, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 October 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 October 2013
Global end of trial reached?	Yes
Global end of trial date	09 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this study were to assess the efficacy and safety of olesoxime 10 milligrams per kilogram (mg/kg) once daily liquid suspension formulation in spinal muscular atrophy (SMA) Type 2 or Type 3 non-ambulant subjects, aged 3 - 25 years.

Protection of trial subjects:

Each subject, or the subject's representative, signed an informed consent form before participating in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 November 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 16
Country: Number of subjects enrolled	France: 29
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	Italy: 52
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	Poland: 20
Country: Number of subjects enrolled	United Kingdom: 19
Worldwide total number of subjects	165
EEA total number of subjects	165

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)	108

Adolescents (12-17 years)	36
Adults (18-64 years)	21
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Eligible subjects included 3 to 25 year-old patients with Type 2 or non-ambulant Type 3 SMA.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Matching placebo, once a day for 104 weeks.

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

Dosage and administration details:

Matching placebo, once a day for 104 weeks.

Arm title	Olesoxime

Arm description:

Olesoxime, 10 mg/kg body weight once a day for 104 weeks.

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

Dosage and administration details:

Olesoxime, 10 mg/kg body weight once a day for 104 weeks.

Number of subjects in period 1	Placebo	Olesoxime
Started	57	108
Completed	50	98
Not completed	7	10
Consent withdrawn by subject	1	3
Adverse event, non-fatal	2	4

Death	1	1
Non-compliance with study drug	1	-
Reason not specified	2	2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Matching placebo, once a day for 104 weeks.	
Reporting group title	Olesoxime
Reporting group description:	
Olesoxime, 10 mg/kg body weight once a day for 104 weeks.	

Reporting group values	Placebo	Olesoxime	Total
Number of subjects	57	108	165
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	30	78	108
Adolescents (12-17 years)	20	16	36
Adults (18-64 years)	7	14	21
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	11.2	9.3	
standard deviation	± 6.0	± 5.7	-
Gender Categorical Units: Subjects			
Female	32	51	83
Male	25	57	82

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Matching placebo, once a day for 104 weeks.	
Reporting group title	Olesoxime
Reporting group description:	
Olesoxime, 10 mg/kg body weight once a day for 104 weeks.	

Primary: Mean Change from Baseline to Week 104 in the Motor Function Measure (MFM) Dimensions 1 and 2 (D1+D2) Score

End point title	Mean Change from Baseline to Week 104 in the Motor Function Measure (MFM) Dimensions 1 and 2 (D1+D2) Score

The MFM is an assessment of functional motor abilities of subjects with neuromuscular disease comprising items rated on a 4-point scale (0 to 3). The MFM items are grouped into three functional dim h r he g D ze e s r A M

End point titcription:

End point title	Change from Baseline in MFM Total Score at Week 104

End point description:

The MFM is an assessment of functional motor abilities of subjects with neuromuscular disease comprising items rated on a 4-point scale (0 to 3). The MFM items are grouped into three functional dimensions D1, D2 and D3. Patient MFM scores were normalized to the maximum achievable score. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Placebo	Olesoxime		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	103		
Units: score				
least squares mean (standard error)	-1.45 (± 0.943)	0.59 (± 0.751)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Hammersmith Functional Motor Scale (HFMS) at Week 91

End point title	Change from Baseline in Hammersmith Functional Motor Scale (HFMS) at Week 91

End point description:

The HFMS consists of 20 items, assessing the subject's ability to perform various activities. Each activity is scored on a 3-point scoring system, with a score of 2 for unaided, 1 for assistance, and 0 for inability. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

End point type	Secondary

End point timeframe:

Baseline to Week 91

End point values	Placebo	Olesoxime		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	103		
Units: score				
least squares mean (standard error)	-1.72 (± 0.515)	-0.78 (± 0.416)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to 4-Point Decrease on the HFMS Score

End point title	Time to 4-Point Decrease on the HFMS Score

End point description:

The HFMS consists of 20 items, assessing the subject's ability to perform various activities. Each activity is scored on a 3-point scoring system, with a score of 2 for unaided, 1 for assistance, and 0 for inability. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available. 9999=not estimable.

End point type	Secondary

End point timeframe:

Up to Week 104

End point values	Placebo	Olesoxime		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	103		
Units: weeks				
median (confidence interval 95%)	9999 (91.4 to 9999)	9999 (9999 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Response for MFM D1+D2 Score at Week 104

End point title	Percentage of Subjects with Response for MFM D1+D2 Score at Week 104

End point description:

The MFM is an assessment of functional motor abilities of subjects with neuromuscular disease comprising items rated on a 4-point scale (0 to 3). The MFM items are grouped into three functional dimensions D1, D2 and D3. Patient MFM scores were normalized to the maximum achievable score. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Placebo	Olesoxime		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	103		
Units: percentage of subjects				
number (not applicable)	38.6	54.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Response for MFM Total Score at Week 104

End point title	Percentage of Subjects with Response for MFM Total Score at Week 104

End point description:

The MFM is an assessment of functional motor abilities of subjects with neuromuscular disease comprising items rated on a 4-point scale (0 to 3). The MFM items are grouped into three functional dimensions D1, D2 and D3. Patient MFM scores were normalized to the maximum achievable score. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Placebo	Olesoxime		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	103		
Units: percentage of subjects				
number (not applicable)	38.6	56.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Response for HFMS Score at Week 91

End point title	Percentage of Subjects with Response for HFMS Score at Week 91

End point description:

The HFMS consists of 20 items, assessing the subject's ability to perform various activities. Each activity is scored on a 3-point scoring system, with a score of 2 for unaided, 1 for assistance, and 0 for inability. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

End point type	Secondary

End point timeframe:

Baseline to Week 91

End point values	Placebo	Olesoxime		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	103		
Units: percentage of subjects				
number (not applicable)	28.1	49.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Compound Muscle Action Potential (CMAP) at Week 104

End point title	Change from Baseline in Compound Muscle Action Potential (CMAP) at Week 104

End point description:

CMAP is an electromyography investigation (electrical study of muscle function). The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

End point type	Secondary

End point timeframe:

Change from Baseline in Compound Muscle Action Potential (CMAP) at Week 104

End point values	Placebo	Olesoxime		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	103		
Units: millivolts (mV)				
least squares mean (standard error)	-0.16 (± 0.294)	-0.07 (± 0.214)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Motor Unit Number Estimation (MUNE) at Week 104

End point title	Change from Baseline in Motor Unit Number Estimation (MUNE) at Week 104

End point description:

MUNE is a technique that can be used to determine the approximate number of motor neurons in a muscle or group of muscles. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Placebo	Olesoxime		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	103		
Units: mune				
least squares mean (standard error)	-6.69 (± 5.106)	-4.51 (± 3.867)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pediatric Quality of Life Inventory (PedsQL) Neuromuscular Module Score - Patient Report

End point title	Change from Baseline in Pediatric Quality of Life Inventory (PedsQL) Neuromuscular Module Score - Patient Report

End point description:

The PedsQL Neuromuscular Module Scales are comprised of parallel child self-report and parent proxy-report formats for children ages 5-18 years, and a parent proxy-report format for children ages 2-4 years. The PedsQL scale assess: the disease process and associated symptoms; the subject's ability to communicate with healthcare providers and others about his/her illness; and items related to family financial and social support systems. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

End point type	Secondary

End point timeframe:

Baseline to Week 104

End point values	Placebo	Olesoxime		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	80		
Units: score				
least squares mean (standard error)	-3.49 (± 2.061)	-3.24 (± 1.729)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in PedsQL Neuromuscular Module Score - Parent/Caregiver Report at Week 104

End point title	Change from Baseline in PedsQL Neuromuscular Module Score - Parent/Caregiver Report at Week 104

End point description:	
The PedsQL Neuromuscular Module Scales are comprised of parallel child self-report and parent proxy-report formats for children ages 5-18 years, and a parent proxy-report format for children ages 2-4 years. The PedsQL scale assess: the disease process and associated symptoms; the subject's ability to communicate with healthcare providers and others about his/her illness; and items related to family financial and social support systems. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.	
End point type	Secondary
End point timeframe:	
Baseline to Week 104	

End point values	Placebo	Olesoxime		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	103		
Units: score				
least squares mean (standard error)	-5.67 (± 1.954)	-2.06 (± 1.564)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Forced Expiratory Vital Capacity (FVC)/Theoretical Capacity (TC) at Week 104

End point title	Change from Baseline in Forced Expiratory Vital Capacity (FVC)/Theoretical Capacity (TC) at Week 104
End point description:	
Pulmonary Function was assessed in subjects 5 years or older by measuring FVC (as percent predicted for age and height). The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.	
End point type	Secondary
End point timeframe:	
Baseline to Week 104	

End point values	Placebo	Olesoxime		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	80		
Units: percent				
least squares mean (standard error)	6.16 (± 2.601)	4.28 (± 2.316)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression of Change - Patient/Caregiver Assessment at Week 104

End point title	Clinical Global Impression of Change - Patient/Caregiver Assessment at Week 104

End point description:

The CGI-C measures global improvement or change and is rated on a 7-point scale, with scores ranging from 1 (very much improved) through to 7 (very much worse). The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

End point type	Secondary

End point timeframe:

Week 104

End point values	Placebo	Olesoxime		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	103		
Units: percentage of subjects				
number (not applicable)				
Very much improved	0.0	1.0		
Much improved	6.1	3.1		
Minimally improved	16.3	20.8		
No change	59.2	66.7		
Minimally worse	12.2	7.3		
Much worse	6.1	1.0		
Very much worse	0.0	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression of Change at Week 104 - Physician Assessment

End point title	Clinical Global Impression of Change at Week 104 - Physician Assessment

End point description:

The CGI-C measures global improvement or change and is rated on a 7-point scale, with scores ranging from 1 (very much improved) through to 7 (very much worse). The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

End point type	Secondary

End point timeframe:

Week 104

End point values	Placebo	Olesoxime		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	103		
Units: percentage of subjects				
number (not applicable)				
Very much improved	0.0	0.0		
Much improved	6.0	1.0		
Minimally improved	8.0	16.7		
No change	66.0	75.0		
Minimally worse	18.0	7.3		
Much worse	2.0	0.0		
Very much worse	0.0	0.0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 2 years.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Matching placebo, once a day for 104 weeks.

Reporting group title	Olesoxime

Reporting group description:

Olesoxime, 10 mg/kg body weight once a day for 104 weeks.

Serious adverse events	Placebo	Olesoxime	
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 57 (50.88%)	34 / 108 (31.48%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events			
Surgical and medical procedures			
Appendicectomy			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthrodesis			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device therapy			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture treatment			

subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrostomy			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hospitalisation			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mechanical ventilation			
subjects affected / exposed	1 / 57 (1.75%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scoliosis surgery			
subjects affected / exposed	2 / 57 (3.51%)	5 / 108 (4.63%)	
occurrences causally related to treatment / all	0 / 2	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fusion surgery			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal operation			
subjects affected / exposed	1 / 57 (1.75%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal rod insertion			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenotomy			

subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth extraction			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 57 (3.51%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Unevaluable event			
subjects affected / exposed	0 / 57 (0.00%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	1 / 57 (1.75%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cough			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoventilation			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	0 / 57 (0.00%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pleurisy			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 57 (3.51%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Restrictive pulmonary disease			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillar hypertrophy			

Oxygen saturation decreased			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary function test			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sleep study			
subjects affected / exposed	0 / 57 (0.00%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 57 (0.00%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	2 / 57 (3.51%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 57 (0.00%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Fracture displacement			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Greenstick fracture			
subjects affected / exposed	1 / 57 (1.75%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Cryptorchism			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Frenulum breve			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Neuralgia			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Coagulopathy			
subjects affected / exposed	2 / 57 (3.51%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	2 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			

subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ketonuria			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kyphoscoliosis			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scoliosis			
subjects affected / exposed	1 / 57 (1.75%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 57 (1.75%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	4 / 57 (7.02%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	1 / 5	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	3 / 57 (5.26%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			
subjects affected / exposed	1 / 57 (1.75%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	6 / 57 (10.53%)	7 / 108 (6.48%)	
occurrences causally related to treatment / all	0 / 7	5 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			

subjects affected / exposed	0 / 57 (0.00%)	4 / 108 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 57 (1.75%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 57 (1.75%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	0 / 57 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Olesoxime	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 57 (91.23%)	96 / 108 (88.89%)	
Investigations			
Weight increased			
subjects affected / exposed	3 / 57 (5.26%)	4 / 108 (3.70%)	
occurrences (all)	3	4	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	5 / 57 (8.77%)	8 / 108 (7.41%)	
occurrences (all)	6	11	
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 57 (22.81%)	22 / 108 (20.37%)	
occurrences (all)	19	57	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 57 (0.00%)	6 / 108 (5.56%)	
occurrences (all)	0	6	
Pyrexia			
subjects affected / exposed	15 / 57 (26.32%)	33 / 108 (30.56%)	
occurrences (all)	22	57	
Unevaluable event			
subjects affected / exposed	5 / 57 (8.77%)	3 / 108 (2.78%)	
occurrences (all)	5	3	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	3 / 57 (5.26%)	3 / 108 (2.78%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	10 / 57 (17.54%)	20 / 108 (18.52%)	
occurrences (all)	18	39	
Abdominal pain upper			
subjects affected / exposed	4 / 57 (7.02%)	8 / 108 (7.41%)	
occurrences (all)	4	11	
Constipation			

subjects affected / exposed	4 / 57 (7.02%)	5 / 108 (4.63%)	
occurrences (all)	6	5	
Diarrhoea			
subjects affected / exposed	12 / 57 (21.05%)	18 / 108 (16.67%)	
occurrences (all)	16	22	
Nausea			
subjects affected / exposed	3 / 57 (5.26%)	9 / 108 (8.33%)	
occurrences (all)	4	18	
Toothache			
subjects affected / exposed	5 / 57 (8.77%)	1 / 108 (0.93%)	
occurrences (all)	5	1	
Vomiting			
subjects affected / exposed	16 / 57 (28.07%)	25 / 108 (23.15%)	
occurrences (all)	25	38	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	16 / 57 (28.07%)	31 / 108 (28.70%)	
occurrences (all)	30	48	
Oropharyngeal pain			
subjects affected / exposed	9 / 57 (15.79%)	16 / 108 (14.81%)	
occurrences (all)	11	30	
Respiratory tract congestion			
subjects affected / exposed	3 / 57 (5.26%)	3 / 108 (2.78%)	
occurrences (all)	4	6	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 57 (12.28%)	2 / 108 (1.85%)	
occurrences (all)	7	2	
Back pain			
subjects affected / exposed	3 / 57 (5.26%)	3 / 108 (2.78%)	
occurrences (all)	3	4	
Joint contracture			
subjects affected / exposed	4 / 57 (7.02%)	5 / 108 (4.63%)	
occurrences (all)	4	5	
Pain in extremity			

subjects affected / exposed	5 / 57 (8.77%)	14 / 108 (12.96%)	
occurrences (all)	6	17	
Scoliosis			
subjects affected / exposed	4 / 57 (7.02%)	12 / 108 (11.11%)	
occurrences (all)	5	13	
Infections and infestations			
Bronchitis			
subjects affected / exposed	17 / 57 (29.82%)	17 / 108 (15.74%)	
occurrences (all)	21	24	
Ear infection			
subjects affected / exposed	2 / 57 (3.51%)	9 / 108 (8.33%)	
occurrences (all)	2	11	
Gastroenteritis			
subjects affected / exposed	8 / 57 (14.04%)	16 / 108 (14.81%)	
occurrences (all)	12	21	
Influenza			
subjects affected / exposed	9 / 57 (15.79%)	10 / 108 (9.26%)	
occurrences (all)	14	26	
Lower respiratory tract infection			
subjects affected / exposed	3 / 57 (5.26%)	3 / 108 (2.78%)	
occurrences (all)	3	12	
Nasopharyngitis			
subjects affected / exposed	15 / 57 (26.32%)	25 / 108 (23.15%)	
occurrences (all)	34	55	
Pharyngitis			
subjects affected / exposed	6 / 57 (10.53%)	15 / 108 (13.89%)	
occurrences (all)	8	19	
Pneumonia			
subjects affected / exposed	3 / 57 (5.26%)	3 / 108 (2.78%)	
occurrences (all)	3	5	
Respiratory tract infection			
subjects affected / exposed	6 / 57 (10.53%)	15 / 108 (13.89%)	
occurrences (all)	10	30	
Rhinitis			
subjects affected / exposed	6 / 57 (10.53%)	14 / 108 (12.96%)	
occurrences (all)	9	18	

Upper respiratory tract infection			
subjects affected / exposed	13 / 57 (22.81%)	22 / 108 (20.37%)	
occurrences (all)	33	36	
Urinary tract infection			
subjects affected / exposed	4 / 57 (7.02%)	4 / 108 (3.70%)	
occurrences (all)	4	4	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 57 (5.26%)	1 / 108 (0.93%)	
occurrences (all)	3	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported