Clinical trial results:
A Randomized, Double Blind, Placebo-Controlled, Study to Assess the Efficacy, Safety, and Tolerability of RO7239361 in Ambulatory Boys with Duchenne Muscular Dystrophy

Summary

EudraCT number	2016-001654-18
Trial protocol	SE DE BE GB ES NL FR IT
Global end of trial date	28 April 2020

Results information

Result version number	v1 (current)
This version publication date	07 November 2020
First version publication date	07 November 2020

Trial information

Trial identification

Sponsor protocol code	WN40227

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03039686
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)	Yes
EMA paediatric investigation plan number(s)	EMEA-001793-PIP01-15
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	28 April 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 April 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to compare the efficacy of RO7239361 to placebo in ambulatory boys with Duchenne muscular dystrophy (DMD). In addition, the safety and tolerability of RO7239361 were assessed.

Protection of trial subjects:

All study subjects and parents, guardians, or legally acceptable representatives were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 July 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 6
Country: Number of subjects enrolled	Australia: 18
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Japan: 17
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	United States: 58
Worldwide total number of subjects	166
EEA total number of subjects	58

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)	166
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited at sites in 13 countries.

Pre-assignment

Screening details:

Ambulatory boys, 6 to 11 years of age, with Duchenne Muscular Dystrophy (DMD) were randomized (1:1:1) to receive either low or high dose of RO7239361 or placebo.

Period 1

Period 1 title	Double-blind Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received matching placebo solution subcutaneously (SC) on specified days of the 48-week double-blind (DB) period. Following the DB period participants received low dose or high dose RO7239361 on specified days for up to 192 weeks during the open-label period followed by 24 weeks of follow-up.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received matching placebo solution subcutaneously (SC) on specified days of the 48-week double-blind period.

Arm title	RO7239361 Low Dose

Arm description:

Participants received low dose RO7239361 SC on specified days of the 48-week DB period. Following the DB period participants received low dose RO7239361 on specified days for up to 192 weeks during the open-label period followed by 24 weeks of follow-up.

Arm type	Experimental
Investigational medicinal product name	RO7239361
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received low dose RO7239361 SC on specified days of the 48-week DB period.

Arm title	RO7239361 High Dose

Arm description:

Participants received high dose RO7239361 SC on specified days of the 48-week DB period. Following the DB period participants received high dose RO7239361 on specified days for up to 192 weeks during the open-label period followed by 24 weeks of follow-up.

Arm type	Experimental

Investigational medicinal product name	RO7239361
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received high dose RO7239361 SC on specified days of the 48-week DB period.

Number of subjects in period 1	Placebo	RO7239361 Low Dose	RO7239361 High Dose
Started	56	55	55
Completed	29	26	32
Not completed	27	29	23
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	2	2	1
Subject Request to Discontinue Study Treatment	1	2	-
Administrative Reason by Sponsor	24	25	21

Period 2

Period 2 title	Open Label Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	RO7239361 Low Dose

Arm description:

Participants received low dose RO7239361 SC on specified days of the 48-week DB period. Following the DB period participants received low dose RO7239361 on specified days for up to 192 weeks during the open-label (OL) period followed by 24 weeks of follow-up.

Arm type	Experimental
Investigational medicinal product name	RO7239361
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received low dose RO7239361 SC on specified days for up to 192 weeks during the open-label period.

Arm title	RO7239361 High Dose

Arm description:

Participants received high dose RO7239361 SC on specified days of the 48-week DB period. Following the DB period participants received high dose RO7239361 on specified days for up to 192 weeks during the open-label (OL) period followed by 24 weeks of follow-up.

Arm type	Experimental
Investigational medicinal product name	RO7239361
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received high dose RO7239361 SC on specified days for up to 192 weeks during the open-label period.

Number of subjects in period 2[1]	RO7239361 Low Dose	RO7239361 High Dose
Started	38	42
Completed	0	0
Not completed	38	42
Consent withdrawn by subject	3	1
Subject Request to Discontinue Study Treatment	1	-
Administrative Reason by Sponsor	34	41

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: Subjects from the placebo arm in the double-blind period entered the RO7239361 Low Dose and High Dose arms in the open label period as indicated.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received matching placebo solution subcutaneously (SC) on specified days of the 48-week double-blind (DB) period. Following the DB period participants received low dose or high dose RO7239361 on specified days for up to 192 weeks during the open-label period followed by 24 weeks of follow-up.	
Reporting group title	RO7239361 Low Dose
Reporting group description:	
Participants received low dose RO7239361 SC on specified days of the 48-week DB period. Following the DB period participants received low dose RO7239361 on specified days for up to 192 weeks during the open-label period followed by 24 weeks of follow-up.	
Reporting group title	RO7239361 High Dose
Reporting group description:	
Participants received high dose RO7239361 SC on specified days of the 48-week DB period. Following the DB period participants received high dose RO7239361 on specified days for up to 192 weeks during the open-label period followed by 24 weeks of follow-up.	

Reporting group values	Placebo	RO7239361 Low Dose	RO7239361 High Dose
Number of subjects	56	55	55
Age Categorical Units: participants			
Children (2-11 years)	56	55	55
Age Continuous Units: years			
arithmetic mean	8.4	8.5	8.4
standard deviation	± 1.7	± 1.8	± 1.5
Sex: Female, Male Units: participants			
Female	0	0	0
Male	56	55	55

Reporting group values	Total		
Number of subjects	166		
Age Categorical Units: participants			
Children (2-11 years)	166		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: participants			
Female	0		
Male	166		

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received matching placebo solution subcutaneously (SC) on specified days of the 48-week double-blind (DB) period. Following the DB period participants received low dose or high dose RO7239361 on specified days for up to 192 weeks during the open-label period followed by 24 weeks of follow-up.

Reporting group title	RO7239361 Low Dose

Reporting group description:

Participants received low dose RO7239361 SC on specified days of the 48-week DB period. Following the DB period participants received low dose RO7239361 on specified days for up to 192 weeks during the open-label period followed by 24 weeks of follow-up.

Reporting group title	RO7239361 High Dose

Reporting group description:

Participants received high dose RO7239361 SC on specified days of the 48-week DB period. Following the DB period participants received high dose RO7239361 on specified days for up to 192 weeks during the open-label period followed by 24 weeks of follow-up.

Reporting group title	RO7239361 Low Dose

Reporting group description:

Participants received low dose RO7239361 SC on specified days of the 48-week DB period. Following the DB period participants received low dose RO7239361 on specified days for up to 192 weeks during the open-label (OL) period followed by 24 weeks of follow-up.

Reporting group title	RO7239361 High Dose

Reporting group description:

Participants received high dose RO7239361 SC on specified days of the 48-week DB period. Following the DB period participants received high dose RO7239361 on specified days for up to 192 weeks during the open-label (OL) period followed by 24 weeks of follow-up.

Subject analysis set title	RO7239361 Low Dose Whole Study
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received low dose SC on specified days of the 48-week DB period. Following the DB period participants received low dose RO7239361 on specified days for up to 192 weeks during the open-label period followed by 24 weeks of follow-up.

Subject analysis set title	RO7239361 High Dose Whole Study
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received high dose SC on specified days of the 48-week DB period. Following the DB period participants received high dose RO7239361 on specified days for up to 192 weeks during the open-label period followed by 24 weeks of follow-up.

Primary: Baseline for the North Star Ambulatory Assessment (NSAA) Total Score

End point title	Baseline for the North Star Ambulatory Assessment (NSAA) Total Score[1]

End point description:

The NSAA is a functional scale specifically designed for ambulant boys with Duchenne muscular dystrophy (DMD) that can provide information about motor function. The NSAA is a 17-item test of standing, ability to transition from lying to sitting, sitting to standing, and other mobility assessments. Each of the 17 items is evaluated on an ordinal scale of 0-2: 0 = unable to achieve independently, 1 = modified method but achieves goal independent of physical assistance from another, or 2 = normal with no obvious modification of activity. Total score range is 0 to 34. Higher scores reflect better performance. Intent-to-Treat (ITT) population included all enrolled participants who received a randomization treatment assignment.

End point type	Primary

End point timeframe:

Baseline

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 analysis was performed for the baseline NSAA total score.

End point values	Placebo	RO7239361 Low Dose	RO7239361 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	55	55	
Units: score on a scale				
arithmetic mean (standard deviation)	23.1 (± 6.4)	24.5 (± 5.5)	22.7 (± 6.7)	

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in the North Star Ambulatory Assessment (NSAA) Total Score at Week 48

End point title	Change from Baseline in the North Star Ambulatory Assessment (NSAA) Total Score at Week 48

End point description:

The NSAA is a functional scale specifically designed for ambulant boys with Duchenne muscular dystrophy (DMD) that can provide information about motor function. The NSAA is a 17-item test of standing, ability to transition from lying to sitting, sitting to standing, and other mobility assessments. Each of the 17 items is evaluated on an ordinal scale of 0-2: 0 = unable to achieve independently, 1 = modified method but achieves goal independent of physical assistance from another, or 2 = normal with no obvious modification of activity. Total score range is 0 to 34. Higher scores reflect better performance. A positive change from baseline indicates an improvement. Based on the mixed-effect model of repeated measures (MMRM). ITT population included all enrolled participants who received a randomization treatment assignment. MMRM analysis included all participants at baseline and the following number of participants by Week 48: Placebo n=30, Low Dose n=29, High Dose n=33.

End point type	Primary

End point timeframe:

Baseline, Week 48

End point values	Placebo	RO7239361 Low Dose	RO7239361 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	55	55	
Units: score on a scale				
least squares mean (standard error)	-2.99 (± 0.65)	-3.44 (± 0.67)	-2.41 (± 0.64)	

Statistical analyses

Statistical analysis title	RO7239361 Low Dose versus Placebo

Statistical analysis description:

Based on the MMRM using an unstructured covariance matrix -change = Baseline + Age Interactive response system (IXRS) Stratum + Corticosteroid Regimen IXRS Stratum + Analysis Visit*Treatment.

Comparison groups	Placebo v RO7239361 Low Dose
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.17
upper limit	1.27
Variability estimate	Standard error of the mean
Dispersion value	0.87

Statistical analysis title	RO7239361 High Dose versus Placebo

Statistical analysis description:

Based on the MMRM using an unstructured covariance matrix -change = Baseline + Age Interactive response system (IXRS) Stratum + Corticosteroid Regimen IXRS Stratum + Analysis Visit*Treatment.

Comparison groups	Placebo v RO7239361 High Dose
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	2.26
Variability estimate	Standard error of the mean
Dispersion value	0.85

Secondary: Baseline Time for 4 Stair Climb

End point title	Baseline Time for 4 Stair Climb

End point description:

The time to complete the 4 stair climb was measured at baseline. ITT population included all enrolled participants who received a randomization treatment assignment.

End point type	Secondary

End point timeframe:

Baseline

End point values	Placebo	RO7239361 Low Dose	RO7239361 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	55	55	
Units: seconds (secs)				
arithmetic mean (standard deviation)	3.81 (± 1.55)	3.85 (± 1.61)	3.92 (± 1.91)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline at Week 48 in the 4 Stair Climb Velocity (4SCV)

End point title	Change from Baseline at Week 48 in the 4 Stair Climb Velocity (4SCV)

End point description:

4SCV was calculated as the ratio of the number of stairs climbed (4) divided by the number of seconds taken to complete the 4-stair climb. The results were converted into velocity (distance/time). A positive change from baseline indicates an improvement. Based on the mixed-effect model of repeated measures (MMRM). ITT population included all enrolled participants who received a randomization treatment assignment. MMRM analysis included all participants at baseline and the following number of participants by Week 48: Placebo n=30, Low Dose n=29, High Dose n=33.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Placebo	RO7239361 Low Dose	RO7239361 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	55	55	
Units: stairs/sec				
least squares mean (standard error)	-0.15 (± 0.07)	-0.15 (± 0.07)	-0.07 (± 0.07)	

Statistical analyses

Statistical analysis title	RO7239361 Low Dose versus Placebo

Statistical analysis description:

Based on the MMRM using an unstructured covariance matrix -change = Baseline + Age Interactive response system (IXRS) Stratum + Corticosteroid Regimen IXRS Stratum + Analysis Visit*Treatment.

Comparison groups	Placebo v RO7239361 Low Dose
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.1

Statistical analysis title	RO7239361 High Dose versus Placebo

Statistical analysis description:

Based on the MMRM using an unstructured covariance matrix -change = Baseline + Age Interactive response system (IXRS) Stratum + Corticosteroid Regimen IXRS Stratum + Analysis Visit*Treatment.

Comparison groups	Placebo v RO7239361 High Dose
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.27
Variability estimate	Standard error of the mean
Dispersion value	0.1

Secondary: Baseline for the Time to Stand from Supine

End point title	Baseline for the Time to Stand from Supine

End point description:

The time required for a participant to stand from supine position. A longer time reflects a worse outcome. ITT population included all enrolled participants who received a randomization treatment assignment.

End point type	Secondary

End point timeframe:

Baseline

End point values	Placebo	RO7239361 Low Dose	RO7239361 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	55	55	
Units: secs				
arithmetic mean (standard deviation)	6.28 (± 4.75)	6.15 (± 4.07)	7.24 (± 9.22)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline at Week 48 in Stand from Supine Velocity

End point title	Change from Baseline at Week 48 in Stand from Supine Velocity

End point description:

The time required for a participant to stand from supine position. A lower velocity reflects a worse outcome. A positive change from baseline indicates an improvement. Based on the mixed-effect model of repeated measures (MMRM). ITT population included all enrolled participants who received a randomization treatment assignment. MMRM analysis included all participants at baseline and the following number of participants by Week 48: Placebo n=28, Low Dose n=28, High Dose n=32.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Placebo	RO7239361 Low Dose	RO7239361 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	55	55	
Units: 1/sec				
least squares mean (standard error)	-0.05 (± 0.01)	-0.02 (± 0.01)	-0.02 (± 0.01)	

Statistical analyses

Statistical analysis title	RO7239361 Low Dose versus Placebo

Statistical analysis description:

Based on the MMRM using an unstructured covariance matrix -change = Baseline + Age Interactive response system (IXRS) Stratum + Corticosteroid Regimen IXRS Stratum + Analysis Visit*Treatment.

Comparison groups	Placebo v RO7239361 Low Dose
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.06

Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	RO7239361 High Dose versus Placebo

Statistical analysis description:

Based on the MMRM using an unstructured covariance matrix -change = Baseline + Age Interactive response system (IXRS) Stratum + Corticosteroid Regimen IXRS Stratum + Analysis Visit*Treatment.

Comparison groups	Placebo v RO7239361 High Dose
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.06
Variability estimate	Standard error of the mean
Dispersion value	0.02

Secondary: Baseline for 10 Meter Walk/Run

End point title	Baseline for 10 Meter Walk/Run

End point description:

The time required for a participant to run or walk a distance of 10 meters as quickly as possible. A longer time reflects a worse outcome. ITT population included all enrolled participants who received a randomization treatment assignment.

End point type	Secondary

End point timeframe:

Baseline

End point values	Placebo	RO7239361 Low Dose	RO7239361 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	55	55	
Units: secs				
arithmetic mean (standard deviation)	5.38 (± 1.48)	5.51 (± 1.68)	5.68 (± 2.30)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline at Week 48 in 10 M Walk/Run Velocity

End point title	Change from Baseline at Week 48 in 10 M Walk/Run Velocity

End point description:

The time required for a participant to run or walk a distance of 10 meters as quickly as possible calculated as velocity (distance/time). A positive change from baseline indicates an improvement. Based on the mixed-effect model of repeated measures (MMRM). ITT population included all enrolled participants who received a randomization treatment assignment. MMRM analysis included all participants at baseline and the following number of participants by Week 48: Placebo n=30, Low Dose n=29, High Dose n=31.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Placebo	RO7239361 Low Dose	RO7239361 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	55	55	
Units: m/sec				
least squares mean (standard error)	-0.23 (± 0.06)	-0.14 (± 0.07)	-0.23 (± 0.06)	

Statistical analyses

Statistical analysis title	RO7239361 Low Dose versus Placebo

Statistical analysis description:

Based on the MMRM using an unstructured covariance matrix -change = Baseline + Age Interactive response system (IXRS) Stratum + Corticosteroid Regimen IXRS Stratum + Analysis Visit*Treatment.

Comparison groups	Placebo v RO7239361 Low Dose
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	0.27
Variability estimate	Standard error of the mean
Dispersion value	0.09

Statistical analysis title	RO7239361 High Dose versus Placebo

Statistical analysis description:

Based on the MMRM using an unstructured covariance matrix -change = Baseline + Age Interactive response system (IXRS) Stratum + Corticosteroid Regimen IXRS Stratum + Analysis Visit*Treatment.

Comparison groups	Placebo v RO7239361 High Dose

Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.17
upper limit	0.18
Variability estimate	Standard error of the mean
Dispersion value	0.09

Secondary: Baseline for the Pediatric Outcome Data Collection Instrument (PODCI) Transfer and Basic Mobility Subscale

End point title	Baseline for the Pediatric Outcome Data Collection Instrument (PODCI) Transfer and Basic Mobility Subscale

End point description:

The PODCI is designed to be completed by the parent/guardian of a child who has knowledge of the child's conditions. The Transfer and Basic Mobility scale is one of the subscales of the PODCI. The results are standardized into a scale of 0-100 with a higher score reflecting better performance. ITT population included all enrolled participants who received a randomization treatment assignment.

End point type	Secondary

End point timeframe:

Baseline

End point values	Placebo	RO7239361 Low Dose	RO7239361 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	55	55	
Units: score on a scale				
arithmetic mean (standard deviation)	85.59 (± 10.21)	86.54 (± 9.52)	84.47 (± 14.76)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline at Week 48 in Pediatric Outcome Data Collection Instrument (PODCI) Transfer and Basic Mobility Subscale

End point title	Change from Baseline at Week 48 in Pediatric Outcome Data Collection Instrument (PODCI) Transfer and Basic Mobility Subscale

End point description:

The PODCI is designed to be completed by the parent/guardian of a child who has knowledge of the child's conditions. The Transfer and Basic Mobility scale is one of the subscales of the PODCI. The results are standardized into a scale of 0-100 with a higher score reflecting better performance. A positive

change from baseline indicates an improvement. Based on the mixed-effect model of repeated measures (MMRM). ITT population included all enrolled participants who received a randomization treatment assignment. MMRM analysis included all participants at baseline and the following number of participants by Week 48: Placebo n=31, Low Dose n=29, High Dose n=34.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Placebo	RO7239361 Low Dose	RO7239361 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	55	55	
Units: score on a scale				
least squares mean (standard error)	-5.47 (± 1.79)	-7.47 (± 1.83)	-4.51 (± 1.77)	

Statistical analyses

Statistical analysis title	RO7239361 Low Dose versus Placebo

Statistical analysis description:

Based on the MMRM using an unstructured covariance matrix -change = Baseline + Age Interactive response system (IXRS) Stratum + Corticosteroid Regimen IXRS Stratum + Analysis Visit*Treatment.

Comparison groups	Placebo v RO7239361 Low Dose
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.76
upper limit	2.77
Variability estimate	Standard error of the mean
Dispersion value	2.41

Statistical analysis title	RO7239361 High Dose versus Placebo

Statistical analysis description:

Based on the MMRM using an unstructured covariance matrix -change = Baseline + Age Interactive response system (IXRS) Stratum + Corticosteroid Regimen IXRS Stratum + Analysis Visit*Treatment.

Comparison groups	Placebo v RO7239361 High Dose

Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.71
upper limit	5.63
Variability estimate	Standard error of the mean
Dispersion value	2.36

Secondary: Change from Baseline at Week 48 in Proximal Lower Extremity Flexor Strength

End point title	Change from Baseline at Week 48 in Proximal Lower Extremity Flexor Strength

End point description:

Proximal lower extremity flexor (knee extension and knee flexion) strength was measured using manual myometry. A higher score reflects a better outcome. A positive change from baseline indicates an improvement. ITT population included all enrolled participants who received a randomization treatment assignment. Number analyzed is the number of participants with data available for analyses at the given timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Placebo	RO7239361 Low Dose	RO7239361 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	55	55	
Units: kilogram (kg)				
arithmetic mean (standard deviation)				
Baseline: Knee Extenders (n=56, 55, 54)	5.58 (± 2.87)	6.25 (± 3.63)	5.76 (± 3.53)	
Change at Week 48: Knee Extenders (n=30, 28, 33)	-1.19 (± 2.13)	-0.47 (± 2.43)	-0.88 (± 2.97)	
Baseline: Knee Flexors (n=56, 55, 54)	5.04 (± 2.58)	5.70 (± 3.08)	5.04 (± 2.72)	
Change at Week 48: Knee Flexors (n=30, 28, 33)	0.15 (± 2.24)	0.08 (± 2.53)	-0.13 (± 2.29)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline for the 6 Minute Walk Distance (6MWD)

End point title	Baseline for the 6 Minute Walk Distance (6MWD)

End point description:

The 6MWD measured the distance a participant was able to traverse while walking for 6 minutes. A longer distance reflects a better outcome. ITT population included all enrolled participants who received a randomization treatment assignment.

End point type	Secondary

End point timeframe:

Baseline

End point values	Placebo	RO7239361 Low Dose	RO7239361 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	55	55	
Units: meters (m)				
arithmetic mean (standard deviation)	388.33 (± 69.59)	399.73 (± 68.35)	370.73 (± 93.35)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline at Week 48 in 6 Minute Walk Distance (6MWD)

End point title	Change from Baseline at Week 48 in 6 Minute Walk Distance (6MWD)

End point description:

The 6MWD measured the distance a participant was able to traverse while walking for 6 minutes. A longer distance reflects a better outcome. A positive change from baseline indicates an improvement. Based on the mixed-effect model of repeated measures (MMRM). ITT population included all enrolled participants who received a randomization treatment assignment. MMRM analysis included all participants at baseline and the following number of participants by Week 48: Placebo n=29, Low Dose n=25, High Dose n=31.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Placebo	RO7239361 Low Dose	RO7239361 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	55	55	
Units: meters (m)				
least squares mean (standard error)	-41.3 (± 8.7)	-39.6 (± 9.0)	-30.0 (± 8.7)	

Statistical analyses

Statistical analysis title	RO7239361 Low Dose versus Placebo

Statistical analysis description:

Based on the MMRM using an unstructured covariance matrix -change = Baseline + Age Interactive response system (IXRS) Stratum + Corticosteroid Regimen IXRS Stratum + Analysis Visit*Treatment.

Comparison groups	Placebo v RO7239361 Low Dose
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.1
upper limit	24.6
Variability estimate	Standard error of the mean
Dispersion value	11.5

Statistical analysis title	RO7239361 High Dose versus Placebo

Statistical analysis description:

Based on the MMRM using an unstructured covariance matrix -change = Baseline + Age Interactive response system (IXRS) Stratum + Corticosteroid Regimen IXRS Stratum + Analysis Visit*Treatment.

Comparison groups	Placebo v RO7239361 High Dose
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	11.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	33.6
Variability estimate	Standard error of the mean
Dispersion value	11.3

Secondary: Percentage of Participants for Each Clinical Global Impression of Change (CGI-C) Assessment Status at Week 48

End point title	Percentage of Participants for Each Clinical Global Impression of Change (CGI-C) Assessment Status at Week 48

End point description:

The CGI-C was used to assess the participant's overall condition on a 7-point scale, using the status markers "very much improved, much improved, slightly improved, no change, slightly worse, much worse or very much worse" at Week 48 as compared to baseline. ITT population included all enrolled participants who received a randomization treatment assignment. Included in the analysis are only those subjects for whom an efficacy assessment was completed at Week 48.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Placebo	RO7239361 Low Dose	RO7239361 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	36	37	31	
Units: percentage of participants				
number (not applicable)				
Very much improved	0	0	0	
Much improved	5.6	2.7	3.2	
Minimally improved	13.9	13.5	19.4	
No change	58.3	54.1	51.6	
Minimally worse	16.7	18.9	22.6	
Much worse	5.6	10.8	3.2	
Very much worse	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline at Week 48 in 95th Percentile Stride Velocity

End point title	Change from Baseline at Week 48 in 95th Percentile Stride Velocity

End point description:

Stride velocity was recorded with the ActiMyo device in a subset of the overall study population. The ActiMyo device measures the daily movement and activity levels of the participant. The device consists of two sensors worn on each ankle. A higher velocity reflects a better outcome. A positive change from baseline indicates an improvement. ITT population included all enrolled participants who received a randomization treatment assignment.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Placebo	RO7239361 Low Dose	RO7239361 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	19	15	
Units: m/sec				
arithmetic mean (standard deviation)				
Baseline (n=17, 19, 15)	1.69 (± 0.33)	1.54 (± 0.35)	1.57 (± 0.46)	
Change from Baseline at Week 48 (n=5, 7, 4)	-0.25 (± 0.39)	-0.22 (± 0.22)	-0.28 (± 0.29)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events (AEs)

End point title	Number of Participants with Adverse Events (AEs)

End point description:

An adverse event is any untoward medical occurrence in a subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered as adverse events. Safety population included all enrolled participants who received at least 1 dose of study therapy. Data are presented for the arms in the DB period as wells as for RO7239361-treated arms in the whole study.

End point type	Secondary

End point timeframe:

During DB period (48 weeks) and Whole study (up to approximately 38 months)

End point values	Placebo	RO7239361 Low Dose	RO7239361 High Dose	RO7239361 Low Dose Whole Study
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	56	55	55	69
Units: participants	46	48	49	57

End point values	RO7239361 High Dose Whole Study			
Subject group type	Subject analysis set			
Number of subjects analysed	68			
Units: participants	56			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with AEs Leading to Discontinuation

End point title	Number of Participants with AEs Leading to Discontinuation

End point description:

An adverse event is any untoward medical occurrence in a subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered as adverse events. Reported here is the number of participants with AEs that led to study discontinuation. Safety population included all enrolled participants who received at least 1 dose of study therapy. Data are presented for the arms in the DB period as wells as for RO7239361-treated arms in the whole study.

End point type	Secondary

End point timeframe:

During DB period (48 weeks) and Whole study (up to approximately 38 months)

End point values	Placebo	RO7239361 Low Dose	RO7239361 High Dose	RO7239361 Low Dose Whole Study
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	56	55	55	69
Units: participants	0	0	0	0

End point values	RO7239361 High Dose Whole Study			
Subject group type	Subject analysis set			
Number of subjects analysed	68			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 38 months

Adverse event reporting additional description:

Safety population included all enrolled participants who received at least 1 dose of study therapy.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Placebo DB

Reporting group description:

Participants received matching placebo solution subcutaneously (SC) on specified days of the 48-week double-blind (DB) period.

Reporting group title	RO7239361 Low Dose DB

Reporting group description:

Participants received low dose RO7239361 SC on specified days of the 48-week DB period.

Reporting group title	RO7239361 High Dose DB

Reporting group description:

Participants received high dose RO7239361 SC on specified days of the 48-week DB period.

Reporting group title	Placebo, Then RO7239361 Low Dose OL

Reporting group description:

Participants received matching placebo solution SC on specified days of the 48-week DB period. Following the DB period participants received low dose RO7239361 on specified days for up to 192 weeks during the open-label (OL) period followed by 24 weeks of follow-up.

Reporting group title	Placebo, Then RO7239361 High Dose OL

Reporting group description:

Participants received matching placebo solution SC on specified days of the 48-week DB period. Following the DB period participants received high dose RO7239361 on specified days for up to 192 weeks during the open-label period followed by 24 weeks of follow-up.

Reporting group title	RO7239361 Low dose, Then RO7239361 Low Dose OL

Reporting group description:

Participants received low dose RO7239361 SC on specified days of the 48-week DB period. Following the DB period participants received low dose RO7239361 on specified days for up to 192 weeks during the open-label period followed by 24 weeks of follow-up.

Reporting group title	RO7239361 High Dose, Then RO7239361 High Dose OL

Reporting group description:

Participants received high dose RO7239361 SC on specified days of the 48-week DB period. Following the DB period participants received high dose RO7239361 on specified days for up to 192 weeks during the open-label period followed by 24 weeks of follow-up

Serious adverse events	Placebo DB	RO7239361 Low Dose DB	RO7239361 High Dose DB
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 56 (5.36%)	2 / 55 (3.64%)	4 / 55 (7.27%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			

Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Myocarditis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastrointestinal viral infection			

subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo, Then RO7239361 Low Dose OL	Placebo, Then RO7239361 High Dose OL	RO7239361 Low dose, Then RO7239361 Low Dose OL
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			

subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastrointestinal viral infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	RO7239361 High Dose, Then RO7239361 High Dose OL		

Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 29 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Overdose			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocarditis			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hyperbilirubinaemia			

subjects affected / exposed	0 / 29 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastrointestinal viral infection			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo DB	RO7239361 Low Dose DB	RO7239361 High Dose DB
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 56 (76.79%)	43 / 55 (78.18%)	47 / 55 (85.45%)
Investigations			
Bone density decreased			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Glutamate dehydrogenase increased			
subjects affected / exposed	2 / 56 (3.57%)	1 / 55 (1.82%)	3 / 55 (5.45%)
occurrences (all)	2	1	3
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 56 (3.57%)	5 / 55 (9.09%)	4 / 55 (7.27%)
occurrences (all)	2	7	5
Fall			

subjects affected / exposed	5 / 56 (8.93%)	1 / 55 (1.82%)	5 / 55 (9.09%)
occurrences (all)	11	1	6
Gadolinium deposition disease			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	4 / 56 (7.14%)	1 / 55 (1.82%)	1 / 55 (1.82%)
occurrences (all)	4	2	1
Skin abrasion			
subjects affected / exposed	2 / 56 (3.57%)	3 / 55 (5.45%)	0 / 55 (0.00%)
occurrences (all)	3	12	0
Thermal burn			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 56 (16.07%)	14 / 55 (25.45%)	10 / 55 (18.18%)
occurrences (all)	28	60	42
Migraine			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	0 / 55 (0.00%)
occurrences (all)	0	10	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 56 (0.00%)	4 / 55 (7.27%)	0 / 55 (0.00%)
occurrences (all)	0	4	0
Gait inability			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Injection site bruising			
subjects affected / exposed	2 / 56 (3.57%)	4 / 55 (7.27%)	4 / 55 (7.27%)
occurrences (all)	3	4	4
Injection site erythema			
subjects affected / exposed	8 / 56 (14.29%)	11 / 55 (20.00%)	12 / 55 (21.82%)
occurrences (all)	25	43	38
Injection site induration			

subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Injection site oedema			
subjects affected / exposed	3 / 56 (5.36%)	2 / 55 (3.64%)	1 / 55 (1.82%)
occurrences (all)	7	9	9
Injection site pruritus			
subjects affected / exposed	0 / 56 (0.00%)	2 / 55 (3.64%)	2 / 55 (3.64%)
occurrences (all)	0	2	6
Injection site reaction			
subjects affected / exposed	2 / 56 (3.57%)	4 / 55 (7.27%)	2 / 55 (3.64%)
occurrences (all)	3	29	33
Injection site swelling			
subjects affected / exposed	0 / 56 (0.00%)	4 / 55 (7.27%)	3 / 55 (5.45%)
occurrences (all)	0	31	5
Localised oedema			
subjects affected / exposed	3 / 56 (5.36%)	0 / 55 (0.00%)	1 / 55 (1.82%)
occurrences (all)	5	0	1
Pyrexia			
subjects affected / exposed	8 / 56 (14.29%)	9 / 55 (16.36%)	8 / 55 (14.55%)
occurrences (all)	8	13	9
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 56 (1.79%)	1 / 55 (1.82%)	4 / 55 (7.27%)
occurrences (all)	1	1	7
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 56 (1.79%)	1 / 55 (1.82%)	1 / 55 (1.82%)
occurrences (all)	2	1	1
Abdominal pain			
subjects affected / exposed	1 / 56 (1.79%)	2 / 55 (3.64%)	3 / 55 (5.45%)
occurrences (all)	1	2	5
Abdominal pain upper			
subjects affected / exposed	3 / 56 (5.36%)	4 / 55 (7.27%)	7 / 55 (12.73%)
occurrences (all)	4	5	12
Constipation			

subjects affected / exposed	4 / 56 (7.14%)	4 / 55 (7.27%)	1 / 55 (1.82%)
occurrences (all)	5	4	1
Diarrhoea			
subjects affected / exposed	3 / 56 (5.36%)	10 / 55 (18.18%)	4 / 55 (7.27%)
occurrences (all)	3	13	8
Dyspepsia			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	3 / 55 (5.45%)
occurrences (all)	0	1	4
Nausea			
subjects affected / exposed	1 / 56 (1.79%)	2 / 55 (3.64%)	5 / 55 (9.09%)
occurrences (all)	1	2	9
Vomiting			
subjects affected / exposed	6 / 56 (10.71%)	8 / 55 (14.55%)	6 / 55 (10.91%)
occurrences (all)	6	14	11
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 56 (17.86%)	8 / 55 (14.55%)	7 / 55 (12.73%)
occurrences (all)	10	11	13
Epistaxis			
subjects affected / exposed	3 / 56 (5.36%)	3 / 55 (5.45%)	6 / 55 (10.91%)
occurrences (all)	9	15	17
Nasal congestion			
subjects affected / exposed	1 / 56 (1.79%)	3 / 55 (5.45%)	3 / 55 (5.45%)
occurrences (all)	1	3	3
Productive cough			
subjects affected / exposed	0 / 56 (0.00%)	3 / 55 (5.45%)	0 / 55 (0.00%)
occurrences (all)	0	3	0
Rhinorrhoea			
subjects affected / exposed	1 / 56 (1.79%)	4 / 55 (7.27%)	3 / 55 (5.45%)
occurrences (all)	1	7	3
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	3 / 56 (5.36%)	2 / 55 (3.64%)	1 / 55 (1.82%)
occurrences (all)	4	2	1
Rash			

subjects affected / exposed	4 / 56 (7.14%)	4 / 55 (7.27%)	7 / 55 (12.73%)
occurrences (all)	9	5	9
Rash macular			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	3 / 56 (5.36%)	2 / 55 (3.64%)	3 / 55 (5.45%)
occurrences (all)	4	2	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 56 (10.71%)	7 / 55 (12.73%)	5 / 55 (9.09%)
occurrences (all)	6	8	6
Back pain			
subjects affected / exposed	4 / 56 (7.14%)	7 / 55 (12.73%)	2 / 55 (3.64%)
occurrences (all)	4	9	2
Mobility decreased			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	1 / 56 (1.79%)	2 / 55 (3.64%)	2 / 55 (3.64%)
occurrences (all)	1	7	6
Pain in extremity			
subjects affected / exposed	2 / 56 (3.57%)	4 / 55 (7.27%)	8 / 55 (14.55%)
occurrences (all)	3	6	11
Infections and infestations			
Ear infection			
subjects affected / exposed	0 / 56 (0.00%)	4 / 55 (7.27%)	1 / 55 (1.82%)
occurrences (all)	0	4	2
Gastroenteritis			
subjects affected / exposed	1 / 56 (1.79%)	1 / 55 (1.82%)	3 / 55 (5.45%)
occurrences (all)	2	1	5
Gastroenteritis viral			
subjects affected / exposed	1 / 56 (1.79%)	1 / 55 (1.82%)	1 / 55 (1.82%)
occurrences (all)	1	1	1
Hordeolum			

subjects affected / exposed	0 / 56 (0.00%)	2 / 55 (3.64%)	0 / 55 (0.00%)
occurrences (all)	0	2	0
Influenza			
subjects affected / exposed	3 / 56 (5.36%)	6 / 55 (10.91%)	1 / 55 (1.82%)
occurrences (all)	3	6	1
Nasopharyngitis			
subjects affected / exposed	13 / 56 (23.21%)	13 / 55 (23.64%)	13 / 55 (23.64%)
occurrences (all)	17	17	16
Pharyngitis			
subjects affected / exposed	2 / 56 (3.57%)	2 / 55 (3.64%)	3 / 55 (5.45%)
occurrences (all)	2	2	3
Rhinitis			
subjects affected / exposed	1 / 56 (1.79%)	3 / 55 (5.45%)	4 / 55 (7.27%)
occurrences (all)	1	5	7
Sinusitis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	3 / 55 (5.45%)
occurrences (all)	1	0	4
Upper respiratory tract infection			
subjects affected / exposed	6 / 56 (10.71%)	4 / 55 (7.27%)	7 / 55 (12.73%)
occurrences (all)	8	5	16

Non-serious adverse events	Placebo, Then RO7239361 Low Dose OL	Placebo, Then RO7239361 High Dose OL	RO7239361 Low dose, Then RO7239361 Low Dose OL
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 14 (57.14%)	7 / 13 (53.85%)	13 / 24 (54.17%)
Investigations			
Bone density decreased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Glutamate dehydrogenase increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	0 / 24 (0.00%)
occurrences (all)	0	2	0

Fall			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Gadolinium deposition disease			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Ligament sprain			
subjects affected / exposed	2 / 14 (14.29%)	0 / 13 (0.00%)	3 / 24 (12.50%)
occurrences (all)	2	0	3
Skin abrasion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	1 / 24 (4.17%)
occurrences (all)	3	0	4
Thermal burn			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	2 / 24 (8.33%)
occurrences (all)	3	0	9
Migraine			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	3
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Gait inability			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Injection site bruising			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	0 / 14 (0.00%)	3 / 13 (23.08%)	2 / 24 (8.33%)
occurrences (all)	0	17	6
Injection site induration			

subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Injection site oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Injection site pruritus			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	0 / 24 (0.00%)
occurrences (all)	0	12	0
Injection site reaction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Injection site swelling			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Localised oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	2 / 14 (14.29%)	1 / 13 (7.69%)	3 / 24 (12.50%)
occurrences (all)	2	1	3
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Constipation			

subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	3 / 24 (12.50%)
occurrences (all)	0	0	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Productive cough			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Rash			

subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Rash macular			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Mobility decreased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	1 / 14 (7.14%)	2 / 13 (15.38%)	0 / 24 (0.00%)
occurrences (all)	1	2	0
Pain in extremity			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Ear infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Hordeolum			

subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2
Nasopharyngitis			
subjects affected / exposed	2 / 14 (14.29%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Pharyngitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	0 / 24 (0.00%)
occurrences (all)	1	1	0

Non-serious adverse events	RO7239361 High Dose, Then RO7239361 High Dose OL		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 29 (41.38%)		
Investigations			
Bone density decreased			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Glutamate dehydrogenase increased			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		

Fall			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Gadolinium deposition disease			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Ligament sprain			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Skin abrasion			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Thermal burn			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	4		
Migraine			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Gait inability			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Injection site bruising			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Injection site erythema			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Injection site induration			

subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Injection site oedema			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Injection site pruritus			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Injection site reaction			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Injection site swelling			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Localised oedema			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	2		
Constipation			

subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Dyspepsia			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	4 / 29 (13.79%)		
occurrences (all)	4		
Vomiting			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	2		
Epistaxis			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Productive cough			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Rash			

subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Rash macular			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Mobility decreased			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Ear infection			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Gastroenteritis viral			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Hordeolum			

subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Pharyngitis			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 April 2017	V1: Added text defining significant change in dosage for prednisone and deflazacort. Added measurement of ulna length to baseline and on treatment time points. Timing of on treatment videotaping of functional assessments was clarified. Timing of Health Care Resource Utilization assessments was clarified. Added clarification that DXA scanning is not required at early termination. History of hypersensitivity of the components of the study drug added as an exclusion. Threshold for adjusting dosing weight tier increased from 1 kg to 2 kg. Text clarifying that malfunctions of pre-filled syringes should be reported to the sponsor in accordance with local regulations has been added. Guidance regarding skin biopsy added. Text describing pharmacogenomics removed.
21 August 2017	V2: Changed Sponsor from Bristol-Myers Squibb to F. Hoffmann-La Roche Ltd. Changed study drug name from BMS-986089 to RO7239361.
29 January 2018	V3: Added assessment of CGI-C. Reduced pulmonary function tests. Reduced anthropometry assessments. Reduced myometry assessments. Reduced timed function tests (TFTs) and 6 minute walk test (6MWT) in the open-label phases. Clarified forced vital capacity (FVC) in the exclusion criteria. Clarified contraception methods. Clarified GDF-11 sample timepoint. Clarified ActiMyo assessments. Clarified use of videos. Updated requirement for safety reporting of overdose. Clarified monitoring of anti-drug antibodies (ADAs) during 24-week safety follow-up phase.
16 August 2018	V4: Deleted references to the previous Bristol-Myers Squibb protocol and product numbers throughout most of the text. Changed the primary endpoint from the 4 Stair Climb velocity (4SCV) to the North Star Ambulatory Assessment total score. Added a new inclusion criterion requiring a minimum NSAA score of 15 points at screening. Changed the 4SCV from the primary endpoint to a secondary endpoint. Added 95th percentile stride velocity, as recorded using the ActiMyo as a secondary endpoint. Updated the duration of the open-label (OL) extension phase and the frequency of visits during the OL extension phase. Added the specific sites indicated for subcutaneous injection. Deleted the proposed interim analysis. Updated the statistical analysis section to establish hierarchical testing of the doses. Added definitions for different situations of incorrect administration of study drug.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
28 April 2020	The study was terminated early as a pre-planned futility analysis indicated lack of efficacy.	-

Notes:

Limitations and caveats

None reported