



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) | EMA-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, Data analyst, Carer, 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 (\pm 1.55) | 3.85 (\pm 1.61) | 3.92 (\pm 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 (\pm 0.07) | -0.15 (\pm 0.07) | -0.07 (\pm 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 (\pm 69.59) | 399.73 (\pm 68.35) | 370.73 (\pm 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 (\pm 8.7) | -39.6 (\pm 9.0) | -30.0 (\pm 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 well 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 well 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 occurrences (all) | 4 / 56 (7.14%) 5 | 4 / 55 (7.27%) 4 | 1 / 55 (1.82%) 1 |
| Diarrhoea subjects affected / exposed occurrences (all) | 3 / 56 (5.36%) 3 | 10 / 55 (18.18%) 13 | 4 / 55 (7.27%) 8 |
| Dyspepsia subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 1 / 55 (1.82%) 1 | 3 / 55 (5.45%) 4 |
| Nausea subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 1 | 2 / 55 (3.64%) 2 | 5 / 55 (9.09%) 9 |
| Vomiting subjects affected / exposed occurrences (all) | 6 / 56 (10.71%) 6 | 8 / 55 (14.55%) 14 | 6 / 55 (10.91%) 11 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 10 / 56 (17.86%) 10 | 8 / 55 (14.55%) 11 | 7 / 55 (12.73%) 13 |
| Epistaxis subjects affected / exposed occurrences (all) | 3 / 56 (5.36%) 9 | 3 / 55 (5.45%) 15 | 6 / 55 (10.91%) 17 |
| Nasal congestion subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 1 | 3 / 55 (5.45%) 3 | 3 / 55 (5.45%) 3 |
| Productive cough subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 3 / 55 (5.45%) 3 | 0 / 55 (0.00%) 0 |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 1 | 4 / 55 (7.27%) 7 | 3 / 55 (5.45%) 3 |
| Skin and subcutaneous tissue disorders | | | |
| Erythema subjects affected / exposed occurrences (all) | 3 / 56 (5.36%) 4 | 2 / 55 (3.64%) 2 | 1 / 55 (1.82%) 1 |
| Rash | | | |

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

| | | | |
|---|------------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 2 / 55 (3.64%) 2 | 0 / 55 (0.00%) 0 |
| Influenza subjects affected / exposed occurrences (all) | 3 / 56 (5.36%) 3 | 6 / 55 (10.91%) 6 | 1 / 55 (1.82%) 1 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 13 / 56 (23.21%) 17 | 13 / 55 (23.64%) 17 | 13 / 55 (23.64%) 16 |
| Pharyngitis subjects affected / exposed occurrences (all) | 2 / 56 (3.57%) 2 | 2 / 55 (3.64%) 2 | 3 / 55 (5.45%) 3 |
| Rhinitis subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 1 | 3 / 55 (5.45%) 5 | 4 / 55 (7.27%) 7 |
| Sinusitis subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 1 | 0 / 55 (0.00%) 0 | 3 / 55 (5.45%) 4 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 6 / 56 (10.71%) 8 | 4 / 55 (7.27%) 5 | 7 / 55 (12.73%) 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 occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 13 (7.69%) 1 | 0 / 24 (0.00%) 0 |
| Glutamate dehydrogenase increased subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 13 (0.00%) 0 | 0 / 24 (0.00%) 0 |
| Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 13 (7.69%) 2 | 0 / 24 (0.00%) 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