



Clinical trial results:

A Phase IIb Randomized, Double-blind, Parallel Group, Placebo- and Active-controlled Study with Double-Blind Extension to Assess the Efficacy and Safety of Vamorolone in Ambulant Boys with Duchenne Muscular Dystrophy (DMD)

Summary

| | |
|--------------------------|----------------------|
| EudraCT number | 2017-002704-27 |
| Trial protocol | BE SE NL CZ GR ES GB |
| Global end of trial date | 06 May 2022 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 15 December 2022 |
| First version publication date | 15 December 2022 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | VBP15-004 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|------------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03439670 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | FDA IND Number: 118942 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | ReveraGen BioPharma Inc. |
| Sponsor organisation address | 155 Gibbs St. Suite 433, Rockville, United States, 20850 |
| Public contact | Chief Operating Officer, ReveraGen BioPharma Inc., +1 215 680 8286, jesse.damsker@reveragen.com |
| Scientific contact | Chief Operating Officer, ReveraGen BioPharma Inc., +1 215 680 8286, jesse.damsker@reveragen.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-001794-PIP02-16 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|-------------|
| Analysis stage | Final |
| Date of interim/final analysis | 06 May 2022 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 06 May 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

1. To compare the efficacy of vamorolone administered orally at daily doses of 6.0 mg/kg over a 24-week treatment period vs. placebo in ambulant boys ages 4 to <7 years with DMD; and
2. To evaluate the safety and tolerability of vamorolone administered orally at daily doses of 2.0 mg/kg and 6.0 mg/kg in ambulant boys ages 4 to <7 years with DMD.

Protection of trial subjects:

The trial will be conducted in accordance with the International Conference on Harmonisation E6 Guideline for Good Clinical Practice; The United States FDA Code of Federal Regulations, Title 21 CFR Part 312, and the US Health Insurance Portability and Accountability Act of 1996. The Parent/guardian of each participant must consent in writing for participant to be enrolled.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 01 March 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Czechia: 8 |
| Country: Number of subjects enrolled | Greece: 5 |
| Country: Number of subjects enrolled | Netherlands: 7 |
| Country: Number of subjects enrolled | Spain: 7 |
| Country: Number of subjects enrolled | Sweden: 3 |
| Country: Number of subjects enrolled | United Kingdom: 30 |
| Country: Number of subjects enrolled | Belgium: 6 |
| Country: Number of subjects enrolled | Australia: 9 |
| Country: Number of subjects enrolled | Israel: 2 |
| Country: Number of subjects enrolled | Canada: 14 |
| Country: Number of subjects enrolled | United States: 30 |
| Worldwide total number of subjects | 121 |
| EEA total number of subjects | 36 |

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) | 121 |
| 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: -

Pre-assignment

Screening details:

The target population for this study was boys with DMD between 4 to <7 years who were corticosteroid naïve and ambulatory.

Period 1

| | |
|------------------------------|---|
| Period 1 title | Period 1 |
| 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 | Treatment Group 1 |

Arm description:

Patients enrolled in Treatment Group 1 (experimental group) will receive vamorolone 2.0 mg/kg/day for 24 weeks followed by vamorolone 2.0mg/kg/day for 20 weeks.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | vamorolone 1.33% wt/wt oral suspension |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects in the vamorolone 2.0 mg/kg were administered a vamorolone 1.33% wt/wt oral suspension. The same volume of either vamorolone 2 or 6 mg/kg or its placebo were orally administered using a volumetric syringe with a breakfast that included at least 8 g of fat; the dose administered was based on the subject's weight at the previous visit. Following administration of the study drug suspension, the volumetric syringe was filled once with water and the water was orally administered.

| | |
|------------------|-------------------|
| Arm title | Treatment Group 2 |
|------------------|-------------------|

Arm description:

Patients enrolled in Treatment Group 2 (experimental group) will receive vamorolone 6.0 mg/kg/day for 24 weeks followed by vamorolone 6.0mg/kg/day for 20 weeks.

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | vamorolone 4.0% wt/wt oral suspension |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects in the vamorolone 6.0 mg/kg group were administered a vamorolone 4.0% wt/wt oral suspension. The same volume of either vamorolone 2 or 6 mg/kg or its placebo were orally administered using a volumetric syringe with a breakfast that included at least 8 g of fat; the dose administered was based on the subject's weight at the previous visit. Following administration of the study drug suspension, the volumetric syringe was filled once with water and the water was orally administered.

| | |
|------------------|-------------------|
| Arm title | Treatment Group 3 |
|------------------|-------------------|

Arm description:

Patients enrolled in Treatment Group 3 (active comparator group) will receive prednisone 0.75 mg/kg/day for 24 weeks followed by vamorolone 2.0mg/kg/day for 20 weeks.

| | |
|--|-------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | 5 mg prednisone tablets |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Prednisone 0.75 mg/kg were administered orally as tablet(s). Prednisone was supplied as 5 mg tablets; the number of prednisone or matching placebo tablets that were administered was based on the subject's weight at the previous visit. Following tablet administration, the subject drank approximately 50 mL (ie, approximately 2 ounces) of water.

| | |
|--|--|
| Investigational medicinal product name | vamorolone 1.33% wt/wt oral suspension |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects in the vamorolone 2.0 mg/kg were administered a vamorolone 1.33% wt/wt oral suspension. The same volume of either vamorolone 2 or 6 mg/kg or its placebo were orally administered using a volumetric syringe with a breakfast that included at least 8 g of fat; the dose administered was based on the subject's weight at the previous visit. Following administration of the study drug suspension, the volumetric syringe was filled once with water and the water was orally administered.

| | |
|------------------|-------------------|
| Arm title | Treatment Group 4 |
|------------------|-------------------|

Arm description:

Patients enrolled in Treatment Group 4 (active comparator group) will receive prednisone 0.75 mg/kg/day for 24 weeks followed by vamorolone 6.0mg/kg/day for 20 weeks.

| | |
|--|-------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | 5 mg prednisone tablets |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Prednisone 0.75 mg/kg were administered orally as tablet(s). Prednisone was supplied as 5 mg tablets; the number of prednisone or matching placebo tablets that were administered was based on the subject's weight at the previous visit. Following tablet administration, the subject drank approximately 50 mL (ie, approximately 2 ounces) of water.

| | |
|--|-----------------------------------|
| Investigational medicinal product name | Placebo for vamorolone suspension |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

The same volume of either vamorolone 2 or 6 mg/kg or its placebo were orally administered using a volumetric syringe with a breakfast that included at least 8 g of fat; the dose administered was based on the subject's weight at the previous visit. Following administration of the study drug suspension, the volumetric syringe was filled once with water and the water was orally administered.

| | |
|------------------|-------------------|
| Arm title | Treatment Group 5 |
|------------------|-------------------|

Arm description:

Patients enrolled in Treatment Group 5 will receive placebo for 24 weeks followed by vamorolone 2mg/kg/day for 20 weeks.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|-----------------------------------|
| Investigational medicinal product name | Placebo for vamorolone suspension |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

The same volume of either vamorolone 2 or 6 mg/kg or its placebo were orally administered using a volumetric syringe with a breakfast that included at least 8 g of fat; the dose administered was based on the subject's weight at the previous visit. Following administration of the study drug suspension, the volumetric syringe was filled once with water and the water was orally administered.

| | |
|--|--|
| Investigational medicinal product name | vamorolone 1.33% wt/wt oral suspension |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects in the vamorolone 2.0 mg/kg were administered a vamorolone 1.33% wt/wt oral suspension. The same volume of either vamorolone 2 or 6 mg/kg or its placebo were orally administered using a volumetric syringe with a breakfast that included at least 8 g of fat; the dose administered was based on the subject's weight at the previous visit. Following administration of the study drug suspension, the volumetric syringe was filled once with water and the water was orally administered.

| | |
|------------------|-------------------|
| Arm title | Treatment Group 6 |
|------------------|-------------------|

Arm description:

Patients enrolled in Treatment Group 6 will receive placebo for 24 weeks followed by vamorolone 6mg/kg/day for 20 weeks.

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo for vamorolone suspension |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

The same volume of either vamorolone 2 or 6 mg/kg or its placebo were orally administered using a volumetric syringe with a breakfast that included at least 8 g of fat; the dose administered was based on the subject's weight at the previous visit. Following administration of the study drug suspension, the volumetric syringe was filled once with water and the water was orally administered.

| | |
|--|---------------------------------------|
| Investigational medicinal product name | vamorolone 4.0% wt/wt oral suspension |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects in the vamorolone 6.0 mg/kg group were administered a vamorolone 4.0% wt/wt oral suspension. The same volume of either vamorolone 2 or 6 mg/kg or its placebo were orally administered using a volumetric syringe with a breakfast that included at least 8 g of fat; the dose administered was based on the subject's weight at the previous visit. Following administration of the study drug suspension, the volumetric syringe was filled once with water and the water was orally administered.

| Number of subjects in period 1 | Treatment Group 1 | Treatment Group 2 | Treatment Group 3 |
|--------------------------------|-------------------|-------------------|-------------------|
| Started | 30 | 30 | 15 |
| Completed | 30 | 30 | 15 |

| Number of subjects in period 1 | Treatment Group 4 | Treatment Group 5 | Treatment Group 6 |
|--------------------------------|-------------------|-------------------|-------------------|
| Started | 16 | 15 | 15 |
| Completed | 16 | 15 | 15 |

Period 2

| | |
|------------------------------|--|
| Period 2 title | Period 2 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer, Assessor |

Arms

| | |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Treatment Group 1 |

Arm description:

Patients enrolled in Treatment Group 1 (experimental group) will receive vamorolone 2.0 mg/kg/day for 24 weeks followed by vamorolone 2.0mg/kg/day for 20 weeks.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | vamorolone 1.33% wt/wt oral suspension |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects in the vamorolone 2.0 mg/kg were administered a vamorolone 1.33% wt/wt oral suspension. The same volume of either vamorolone 2 or 6 mg/kg or its placebo were orally administered using a volumetric syringe with a breakfast that included at least 8 g of fat; the dose administered was based on the subject's weight at the previous visit. Following administration of the study drug suspension, the volumetric syringe was filled once with water and the water was orally administered.

| | |
|------------------|-------------------|
| Arm title | Treatment Group 2 |
|------------------|-------------------|

Arm description:

Patients enrolled in Treatment Group 2 (experimental group) will receive vamorolone 6.0 mg/kg/day for 24 weeks followed by vamorolone 6.0mg/kg/day for 20 weeks.

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | vamorolone 4.0% wt/wt oral suspension |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects in the vamorolone 6.0 mg/kg group were administered a vamorolone 4.0% wt/wt oral

suspension. The same volume of either vamorolone 2 or 6 mg/kg or its placebo were orally administered using a volumetric syringe with a breakfast that included at least 8 g of fat; the dose administered was based on the subject's weight at the previous visit. Following administration of the study drug suspension, the volumetric syringe was filled once with water and the water was orally administered.

| | |
|------------------|-------------------|
| Arm title | Treatment Group 3 |
|------------------|-------------------|

Arm description:

Patients enrolled in Treatment Group 3 (active comparator group) will receive prednisone 0.75 mg/kg/day for 24 weeks followed by vamorolone 2.0mg/kg/day for 20 weeks.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | vamorolone 1.33% wt/wt oral suspension |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects in the vamorolone 2.0 mg/kg were administered a vamorolone 1.33% wt/wt oral suspension. The same volume of either vamorolone 2 or 6 mg/kg or its placebo were orally administered using a volumetric syringe with a breakfast that included at least 8 g of fat; the dose administered was based on the subject's weight at the previous visit. Following administration of the study drug suspension, the volumetric syringe was filled once with water and the water was orally administered.

| | |
|--|-------------------------|
| Investigational medicinal product name | 5 mg prednisone tablets |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Prednisone 0.75 mg/kg were administered orally as tablet(s). Prednisone was supplied as 5 mg tablets; the number of prednisone or matching placebo tablets that were administered was based on the subject's weight at the previous visit. Following tablet administration, the subject drank approximately 50 mL (ie, approximately 2 ounces) of water.

| | |
|------------------|-------------------|
| Arm title | Treatment Group 4 |
|------------------|-------------------|

Arm description:

Patients enrolled in Treatment Group 4 (active comparator group) will receive prednisone 0.75 mg/kg/day for 24 weeks followed by vamorolone 6.0mg/kg/day for 20 weeks.

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | vamorolone 4.0% wt/wt oral suspension |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects in the vamorolone 6.0 mg/kg group were administered a vamorolone 4.0% wt/wt oral suspension. The same volume of either vamorolone 2 or 6 mg/kg or its placebo were orally administered using a volumetric syringe with a breakfast that included at least 8 g of fat; the dose administered was based on the subject's weight at the previous visit. Following administration of the study drug suspension, the volumetric syringe was filled once with water and the water was orally administered.

| | |
|------------------|-------------------|
| Arm title | Treatment Group 5 |
|------------------|-------------------|

Arm description:

Patients enrolled in Treatment Group 5 will receive placebo for 24 weeks followed by vamorolone 2mg/kg/day for 20 weeks.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|-----------------------------------|
| Investigational medicinal product name | Placebo for vamorolone suspension |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

The same volume of either vamorolone 2 or 6 mg/kg or its placebo were orally administered using a volumetric syringe with a breakfast that included at least 8 g of fat; the dose administered was based on the subject's weight at the previous visit. Following administration of the study drug suspension, the volumetric syringe was filled once with water and the water was orally administered.

| | |
|--|--|
| Investigational medicinal product name | vamorolone 1.33% wt/wt oral suspension |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects in the vamorolone 2.0 mg/kg were administered a vamorolone 1.33% wt/wt oral suspension. The same volume of either vamorolone 2 or 6 mg/kg or its placebo were orally administered using a volumetric syringe with a breakfast that included at least 8 g of fat; the dose administered was based on the subject's weight at the previous visit. Following administration of the study drug suspension, the volumetric syringe was filled once with water and the water was orally administered.

| | |
|------------------|-------------------|
| Arm title | Treatment Group 6 |
|------------------|-------------------|

Arm description:

Patients enrolled in Treatment Group 6 will receive placebo for 24 weeks followed by vamorolone 6mg/kg/day for 20 weeks.

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo for vamorolone suspension |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

The same volume of either vamorolone 2 or 6 mg/kg or its placebo were orally administered using a volumetric syringe with a breakfast that included at least 8 g of fat; the dose administered was based on the subject's weight at the previous visit. Following administration of the study drug suspension, the volumetric syringe was filled once with water and the water was orally administered.

| | |
|--|---------------------------------------|
| Investigational medicinal product name | vamorolone 4.0% wt/wt oral suspension |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects in the vamorolone 6.0 mg/kg group were administered a vamorolone 4.0% wt/wt oral suspension. The same volume of either vamorolone 2 or 6 mg/kg or its placebo were orally administered using a volumetric syringe with a breakfast that included at least 8 g of fat; the dose administered was based on the subject's weight at the previous visit. Following administration of the study drug suspension, the volumetric syringe was filled once with water and the water was orally administered.

| Number of subjects in period 2 | Treatment Group 1 | Treatment Group 2 | Treatment Group 3 |
|---------------------------------------|-------------------|-------------------|-------------------|
| Started | 30 | 30 | 15 |
| Completed | 28 | 26 | 15 |
| Not completed | 2 | 4 | 0 |
| Consent withdrawn by subject | 2 | 2 | - |
| Physician decision | - | 1 | - |
| WITHDRAWN DUE TO GH DEFICIENCY | - | - | - |
| Adverse event, non-fatal | - | 1 | - |
| AMBIGUOUS VARICELLA ZOSTER IMMUNITY | - | - | - |

| Number of subjects in period 2 | Treatment Group 4 | Treatment Group 5 | Treatment Group 6 |
|---------------------------------------|-------------------|-------------------|-------------------|
| Started | 16 | 15 | 15 |
| Completed | 15 | 14 | 14 |
| Not completed | 1 | 1 | 1 |
| Consent withdrawn by subject | - | - | - |
| Physician decision | - | - | - |
| WITHDRAWN DUE TO GH DEFICIENCY | - | - | 1 |
| Adverse event, non-fatal | 1 | - | - |
| AMBIGUOUS VARICELLA ZOSTER IMMUNITY | - | 1 | - |

Baseline characteristics

Reporting groups

| | |
|--|-------------------|
| Reporting group title | Treatment Group 1 |
| Reporting group description: | |
| Patients enrolled in Treatment Group 1 (experimental group) will receive vamorolone 2.0 mg/kg/day for 24 weeks followed by vamorolone 2.0mg/kg/day for 20 weeks. | |
| Reporting group title | Treatment Group 2 |
| Reporting group description: | |
| Patients enrolled in Treatment Group 2 (experimental group) will receive vamorolone 6.0 mg/kg/day for 24 weeks followed by vamorolone 6.0mg/kg/day for 20 weeks. | |
| Reporting group title | Treatment Group 3 |
| Reporting group description: | |
| Patients enrolled in Treatment Group 3 (active comparator group) will receive prednisone 0.75 mg/kg/day for 24 weeks followed by vamorolone 2.0mg/kg/day for 20 weeks. | |
| Reporting group title | Treatment Group 4 |
| Reporting group description: | |
| Patients enrolled in Treatment Group 4 (active comparator group) will receive prednisone 0.75 mg/kg/day for 24 weeks followed by vamorolone 6.0mg/kg/day for 20 weeks. | |
| Reporting group title | Treatment Group 5 |
| Reporting group description: | |
| Patients enrolled in Treatment Group 5 will receive placebo for 24 weeks followed by vamorolone 2mg/kg/day for 20 weeks. | |
| Reporting group title | Treatment Group 6 |
| Reporting group description: | |
| Patients enrolled in Treatment Group 6 will receive placebo for 24 weeks followed by vamorolone 6mg/kg/day for 20 weeks. | |

| Reporting group values | Treatment Group 1 | Treatment Group 2 | Treatment Group 3 |
|--|-------------------|-------------------|-------------------|
| Number of subjects | 30 | 30 | 15 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 30 | 30 | 15 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 5.29 | 5.42 | 5.41 |
| full range (min-max) | 4.1 to 7.0 | 4.1 to 6.8 | 4.0 to 6.9 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 30 | 30 | 15 |

| Reporting group values | Treatment Group 4 | Treatment Group 5 | Treatment Group 6 |
|---|-------------------|-------------------|-------------------|
| Number of subjects | 16 | 15 | 15 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 16 | 15 | 15 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 5.61 | 5.35 | 5.44 |
| full range (min-max) | 4.5 to 7.0 | 4.3 to 6.5 | 4.1 to 7.0 |
| Gender categorical Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 16 | 15 | 15 |

| Reporting group values | Total | | |
|---|-------|--|--|
| Number of subjects | 121 | | |
| Age categorical Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 121 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age continuous Units: years | | | |
| arithmetic mean | | | |
| full range (min-max) | - | | |
| Gender categorical Units: Subjects | | | |
| Female | 0 | | |
| Male | 121 | | |

Subject analysis sets

| | |
|----------------------------|------------------|
| Subject analysis set title | Analysis Group 1 |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Patients enrolled in Analysis Group 1 (placebo comparator group) will receive placebo for 24 weeks.

| | |
|----------------------------|------------------|
| Subject analysis set title | Analysis Group 2 |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Patients enrolled in Treatment Group 2 (experimental group) will receive vamorolone 6.0 mg/kg/day for 24 weeks

| Reporting group values | Analysis Group 1 | Analysis Group 2 | |
|--|--------------------|--------------------|--|
| Number of subjects | 28 | 27 | |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: years arithmetic mean full range (min-max) | 5.40 4.1 to 7.0 | 5.42 4.1 to 6.8 | |
| Gender categorical Units: Subjects | | | |
| Female Male | | | |

End points

End points reporting groups

| | |
|--|-------------------|
| Reporting group title | Treatment Group 1 |
| Reporting group description: Patients enrolled in Treatment Group 1 (experimental group) will receive vamorolone 2.0 mg/kg/day for 24 weeks followed by vamorolone 2.0mg/kg/day for 20 weeks. | |
| Reporting group title | Treatment Group 2 |
| Reporting group description: Patients enrolled in Treatment Group 2 (experimental group) will receive vamorolone 6.0 mg/kg/day for 24 weeks followed by vamorolone 6.0mg/kg/day for 20 weeks. | |
| Reporting group title | Treatment Group 3 |
| Reporting group description: Patients enrolled in Treatment Group 3 (active comparator group) will receive prednisone 0.75 mg/kg/day for 24 weeks followed by vamorolone 2.0mg/kg/day for 20 weeks. | |
| Reporting group title | Treatment Group 4 |
| Reporting group description: Patients enrolled in Treatment Group 4 (active comparator group) will receive prednisone 0.75 mg/kg/day for 24 weeks followed by vamorolone 6.0mg/kg/day for 20 weeks. | |
| Reporting group title | Treatment Group 5 |
| Reporting group description: Patients enrolled in Treatment Group 5 will receive placebo for 24 weeks followed by vamorolone 2mg/kg/day for 20 weeks. | |
| Reporting group title | Treatment Group 6 |
| Reporting group description: Patients enrolled in Treatment Group 6 will receive placebo for 24 weeks followed by vamorolone 6mg/kg/day for 20 weeks. | |
| Reporting group title | Treatment Group 1 |
| Reporting group description: Patients enrolled in Treatment Group 1 (experimental group) will receive vamorolone 2.0 mg/kg/day for 24 weeks followed by vamorolone 2.0mg/kg/day for 20 weeks. | |
| Reporting group title | Treatment Group 2 |
| Reporting group description: Patients enrolled in Treatment Group 2 (experimental group) will receive vamorolone 6.0 mg/kg/day for 24 weeks followed by vamorolone 6.0mg/kg/day for 20 weeks. | |
| Reporting group title | Treatment Group 3 |
| Reporting group description: Patients enrolled in Treatment Group 3 (active comparator group) will receive prednisone 0.75 mg/kg/day for 24 weeks followed by vamorolone 2.0mg/kg/day for 20 weeks. | |
| Reporting group title | Treatment Group 4 |
| Reporting group description: Patients enrolled in Treatment Group 4 (active comparator group) will receive prednisone 0.75 mg/kg/day for 24 weeks followed by vamorolone 6.0mg/kg/day for 20 weeks. | |
| Reporting group title | Treatment Group 5 |
| Reporting group description: Patients enrolled in Treatment Group 5 will receive placebo for 24 weeks followed by vamorolone 2mg/kg/day for 20 weeks. | |
| Reporting group title | Treatment Group 6 |
| Reporting group description: Patients enrolled in Treatment Group 6 will receive placebo for 24 weeks followed by vamorolone 6mg/kg/day for 20 weeks. | |
| Subject analysis set title | Analysis Group 1 |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Patients enrolled in Analysis Group 1 (placebo comparator group) will receive placebo for 24 weeks.

| | |
|----------------------------|------------------|
| Subject analysis set title | Analysis Group 2 |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Patients enrolled in Treatment Group 2 (experimental group) will receive vamorolone 6.0 mg/kg/day for 24 weeks

Primary: TTSTAND Velocity Change from Baseline to Week 24: Vamorolone 6 mg/kg versus Placebo

| | |
|-----------------|--|
| End point title | TTSTAND Velocity Change from Baseline to Week 24: Vamorolone 6 mg/kg versus Placebo |
|-----------------|--|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Week 24

| End point values | Analysis Group 1 | Analysis Group 2 | | |
|--------------------------------------|------------------------|-----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 28 | 27 | | |
| Units: rises/second | | | | |
| arithmetic mean (standard deviation) | -0.007 (\pm 0.0628) | 0.054 (\pm 0.0666) | | |

Statistical analyses

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Primary endpoint analysis |
|-----------------------------------|---------------------------|

Statistical analysis description:

For EMA, change from baseline in TTSTAND velocity was compared using the REML-based MMRM and multiple imputation assuming missing not at random (MNAR).

| | |
|---|-------------------------------------|
| Comparison groups | Analysis Group 2 v Analysis Group 1 |
| Number of subjects included in analysis | 55 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0018 |
| Method | Mixed models analysis |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

48 weeks

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 21.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | Treatment Group 1 |
|-----------------------|-------------------|

Reporting group description:

Patients enrolled in Treatment Group 1 (experimental group) will receive vamorolone 2.0 mg/kg/day for 24 weeks followed by vamorolone 2.0mg/kg/day for 20 weeks.

| | |
|-----------------------|-------------------|
| Reporting group title | Treatment Group 2 |
|-----------------------|-------------------|

Reporting group description:

Patients enrolled in Treatment Group 2 (experimental group) will receive vamorolone 6.0 mg/kg/day for 24 weeks followed by vamorolone 6.0mg/kg/day for 20 weeks.

| | |
|-----------------------|-------------------|
| Reporting group title | Treatment Group 3 |
|-----------------------|-------------------|

Reporting group description:

Patients enrolled in Treatment Group 3 (active comparator group) will receive prednisone 0.75 mg/kg/day for 24 weeks followed by vamorolone 2.0mg/kg/day for 20 weeks.

| | |
|-----------------------|-------------------|
| Reporting group title | Treatment Group 4 |
|-----------------------|-------------------|

Reporting group description:

Patients enrolled in Treatment Group 4 (active comparator group) will receive prednisone 0.75 mg/kg/day for 24 weeks followed by vamorolone 6.0mg/kg/day for 20 weeks.

| | |
|-----------------------|-------------------|
| Reporting group title | Treatment Group 5 |
|-----------------------|-------------------|

Reporting group description:

Patients enrolled in Treatment Group 5 will receive placebo for 24 weeks followed by vamorolone 2mg/kg/day for 20 weeks.

| | |
|-----------------------|-------------------|
| Reporting group title | Treatment Group 6 |
|-----------------------|-------------------|

Reporting group description:

Patients enrolled in Treatment Group 6 will receive placebo for 24 weeks followed by vamorolone 6mg/kg/day for 20 weeks.

| Serious adverse events | Treatment Group 1 | Treatment Group 2 | Treatment Group 3 |
|---|-------------------|-------------------|-------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 2 / 28 (7.14%) | 0 / 15 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 28 (3.57%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Infections and infestations | | | |
| Gastroenteritis viral/viral gastroenteritis | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 28 (3.57%) | 0 / 15 (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 |

| Serious adverse events | Treatment Group 4 | Treatment Group 5 | Treatment Group 6 |
|---|-------------------|-------------------|-------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 0 / 14 (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 | | | |
| Gastroenteritis viral/viral gastroenteritis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 0 / 14 (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 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 0 / 14 (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 |

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

| Non-serious adverse events | Treatment Group 1 | Treatment Group 2 | Treatment Group 3 |
|--|--|---|---|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 26 / 28 (92.86%) | 26 / 28 (92.86%) | 15 / 15 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Skin papilloma subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Vascular disorders Hot flush subjects affected / exposed occurrences (all) Peripheral coldness subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 0 / 28 (0.00%) 0 | 0 / 28 (0.00%) 0 0 / 28 (0.00%) 0 | 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 |
| General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Impaired healing subjects affected / exposed occurrences (all) Thirst subjects affected / exposed occurrences (all) | 7 / 28 (25.00%) 8 0 / 28 (0.00%) 0 1 / 28 (3.57%) 1 0 / 28 (0.00%) 0 0 / 28 (0.00%) 0 | 3 / 28 (10.71%) 3 0 / 28 (0.00%) 0 0 / 28 (0.00%) 0 0 / 28 (0.00%) 0 | 3 / 15 (20.00%) 5 0 / 15 (0.00%) 0 2 / 15 (13.33%) 2 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Nasal congestion | 5 / 28 (17.86%) 8 | 3 / 28 (10.71%) 3 | 2 / 15 (13.33%) 2 |

| | | | |
|-----------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 28 (0.00%) | 2 / 28 (7.14%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 2 | 1 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 1 / 28 (3.57%) | 0 / 15 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 28 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Psychiatric disorders | | | |
| Abnormal behaviour | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 1 / 28 (3.57%) | 2 / 15 (13.33%) |
| occurrences (all) | 2 | 1 | 2 |
| Aggression | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 1 / 28 (3.57%) | 0 / 15 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Irritability | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 3 / 28 (10.71%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 3 | 1 |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 28 (3.57%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Anger | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Dysphemia | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Emotional disorder | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Enuresis | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Initial insomnia | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-------------------------------|----------------|-----------------|----------------|
| Insomnia | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mood swings | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oppositional defiant disorder | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Personality change | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Trichotillomania | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 28 (3.57%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Blood uric acid increased | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Protein Urine Present | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 28 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Weight increased | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 3 / 28 (10.71%) | 1 / 15 (6.67%) |
| occurrences (all) | 1 | 3 | 1 |
| Cortisol decreased | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 1 / 28 (3.57%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Bacterial test positive | | | |

| | | | |
|--|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood pressure increased | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 28 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram abnormal | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Glycosylated haemoglobin increased | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lipase decreased | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urine analysis abnormal | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Arthropod bite | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 2 / 28 (7.14%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Contusion | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 1 / 28 (3.57%) | 1 / 15 (6.67%) |
| occurrences (all) | 2 | 1 | 1 |
| Fall | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 4 / 28 (14.29%) | 2 / 15 (13.33%) |
| occurrences (all) | 2 | 5 | 3 |
| Ligament strain | | | |

| | | | |
|---|----------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | 1 / 28 (3.57%) 1 | 0 / 15 (0.00%) 0 |
| Back injury subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Muscle strain subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | 0 / 28 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Vaccination complication subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 15 (6.67%) 2 |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 3 / 28 (10.71%) 3 | 2 / 28 (7.14%) 2 | 1 / 15 (6.67%) 1 |
| Psychomotor hyperactivity subjects affected / exposed occurrences (all) | 2 / 28 (7.14%) 2 | 0 / 28 (0.00%) 0 | 1 / 15 (6.67%) 1 |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Poor quality sleep subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | 0 / 28 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Seizure subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Syncope subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Leukopenia subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Ear and labyrinth disorders | | | |

| | | | |
|-------------------------------|-----------------|-----------------|-----------------|
| Ear pain | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 28 (3.57%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 2 | 1 |
| Tympanic membrane perforation | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal Pain | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | 3 / 28 (10.71%) | 2 / 15 (13.33%) |
| occurrences (all) | 3 | 3 | 3 |
| Abdominal Pain upper | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 3 / 28 (10.71%) | 3 / 15 (20.00%) |
| occurrences (all) | 2 | 6 | 3 |
| Constipation | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | 3 / 28 (10.71%) | 0 / 15 (0.00%) |
| occurrences (all) | 5 | 4 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | 5 / 28 (17.86%) | 1 / 15 (6.67%) |
| occurrences (all) | 3 | 7 | 2 |
| Vomiting | | | |
| subjects affected / exposed | 6 / 28 (21.43%) | 6 / 28 (21.43%) | 1 / 15 (6.67%) |
| occurrences (all) | 8 | 6 | 1 |
| Mouth Ulceration | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 2 / 28 (7.14%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Toothache | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 1 / 28 (3.57%) | 1 / 15 (6.67%) |
| occurrences (all) | 1 | 1 | 1 |
| Diarrhoea haemorrhagic | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |

| | | | |
|---|---------------------|----------------------|----------------------|
| Hepatomegaly subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| Hypertrichosis subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | 3 / 28 (10.71%) 3 | 1 / 15 (6.67%) 1 |
| Rash subjects affected / exposed occurrences (all) | 2 / 28 (7.14%) 2 | 2 / 28 (7.14%) 2 | 2 / 15 (13.33%) 2 |
| Eczema subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 1 / 28 (3.57%) 1 | 0 / 15 (0.00%) 0 |
| Perioral dermatitis subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 1 / 28 (3.57%) 2 | 0 / 15 (0.00%) 0 |
| Pruritis subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 1 / 28 (3.57%) 1 | 1 / 15 (6.67%) 1 |
| Dry skin subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | 0 / 28 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Erythema subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | 0 / 28 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Rash macropapular subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 15 (6.67%) 1 |
| Urticaria subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Viral rash subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Renal and urinary disorders | | | |

| | | | |
|---|----------------------|----------------------|----------------------|
| Chromaturia subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 1 / 28 (3.57%) 1 | 1 / 15 (6.67%) 1 |
| Proteinuria subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | 0 / 28 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Endocrine disorders | | | |
| Cushingoid subjects affected / exposed occurrences (all) | 4 / 28 (14.29%) 4 | 9 / 28 (32.14%) 9 | 4 / 15 (26.67%) 4 |
| Growth hormone deficiency subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 2 / 28 (7.14%) 2 | 3 / 28 (10.71%) 3 | 4 / 15 (26.67%) 5 |
| Back pain subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | 2 / 28 (7.14%) 3 | 0 / 15 (0.00%) 0 |
| Athralgia subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | 1 / 28 (3.57%) 1 | 1 / 15 (6.67%) 1 |
| Muscle spasms subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 1 / 28 (3.57%) 1 | 1 / 15 (6.67%) 1 |
| Myalgia subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 1 / 28 (3.57%) 1 | 0 / 15 (0.00%) 0 |
| Costrochondritis subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Joint contracture subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Joint swelling | | | |

| | | | |
|-----------------------------------|------------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle atrophy | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vertebral wedging | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Agitation | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 28 (3.57%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 28 (3.57%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 1 | 2 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 4 / 28 (14.29%) | 3 / 15 (20.00%) |
| occurrences (all) | 2 | 8 | 5 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 10 / 28 (35.71%) | 4 / 28 (14.29%) | 2 / 15 (13.33%) |
| occurrences (all) | 12 | 7 | 2 |
| Rhinitis | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 4 / 28 (14.29%) | 0 / 15 (0.00%) |
| occurrences (all) | 3 | 5 | 0 |
| Enterobiasis | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 2 / 28 (7.14%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |

| | | | |
|--|-----------------|----------------|-----------------|
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 28 (3.57%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ear Infection | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 1 / 28 (3.57%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 28 (3.57%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 1 | 2 |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 1 / 28 (3.57%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Viral Infection | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 28 (3.57%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Fungal Infection | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastroenteritis viral/viral gastroenteritis | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | 0 / 28 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 3 | 0 | 1 |
| Hand-foot-and-mouth disease | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Impetigo | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Influenza | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 28 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Moluscum contagiosum | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis media bacterial | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 28 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 4 | 0 | 2 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory track infection viral | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Streptococcal infection | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Increased appetite | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 2 / 28 (7.14%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Vitamin D Deficiency | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 3 / 28 (10.71%) | 1 / 15 (6.67%) |
| occurrences (all) | 2 | 5 | 1 |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Overweight | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Polydipsia | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 28 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | Treatment Group 4 | Treatment Group 5 | Treatment Group 6 |
|---|-------------------|-------------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 13 / 15 (86.67%) | 12 / 14 (85.71%) | 14 / 14 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Skin papilloma | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 0 | 1 |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Peripheral coldness | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 3 / 14 (21.43%) | 3 / 14 (21.43%) |
| occurrences (all) | 1 | 3 | 6 |
| Asthenia | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 2 / 15 (13.33%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Impaired healing | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Thirst | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 4 / 15 (26.67%) | 0 / 14 (0.00%) | 2 / 14 (14.29%) |
| occurrences (all) | 4 | 0 | 3 |
| Nasal congestion | | | |
| subjects affected / exposed | 2 / 15 (13.33%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 2 | 0 | 1 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 1 | 0 | 2 |
| Psychiatric disorders | | | |
| Abnormal behaviour | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 14 (7.14%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 2 | 1 |
| Aggression | | | |
| subjects affected / exposed | 2 / 15 (13.33%) | 1 / 14 (7.14%) | 0 / 14 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Irritability | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 0 | 1 |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 14 (7.14%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Anger | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dysphemia | | | |

| | | | |
|-------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Emotional disorder | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Enuresis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 14 (7.14%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Initial insomnia | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 0 | 1 |
| Mood swings | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 1 / 14 (7.14%) | 0 / 14 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Oppositional defiant disorder | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Personality change | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Trichotillomania | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 1 / 14 (7.14%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Investigations | | | |
| Blood uric acid increased | | | |
| subjects affected / exposed | 2 / 15 (13.33%) | 0 / 14 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 3 | 0 | 1 |

| | | | |
|--|----------------------|---------------------|---------------------|
| Protein Urine Present subjects affected / exposed occurrences (all) | 3 / 15 (20.00%) 3 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Weight increased subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 1 / 14 (7.14%) 1 | 1 / 14 (7.14%) 1 |
| Cortisol decreased subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 14 (7.14%) 1 |
| Bacterial test positive subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Blood pressure increased subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 14 (7.14%) 1 | 0 / 14 (0.00%) 0 |
| Blood triglycerides increased subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 14 (7.14%) 1 | 0 / 14 (0.00%) 0 |
| Electrocardiogram abnormal subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Glycosylated haemoglobin increased subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Lipase decreased subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Urine analysis abnormal subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Weight decreased subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 14 (7.14%) 1 |
| Injury, poisoning and procedural complications | | | |

| | | | |
|-----------------------------|-----------------|----------------|-----------------|
| Arthropod bite | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 14 (7.14%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 1 | 3 |
| Contusion | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fall | | | |
| subjects affected / exposed | 3 / 15 (20.00%) | 0 / 14 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 5 | 0 | 1 |
| Ligament strain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 14 (7.14%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Back injury | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Muscle strain | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vaccination complication | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 3 / 14 (21.43%) |
| occurrences (all) | 1 | 0 | 7 |
| Psychomotor hyperactivity | | | |
| subjects affected / exposed | 2 / 15 (13.33%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 0 | 1 |
| Poor quality sleep | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Seizure | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 14 (7.14%) 1 | 0 / 14 (0.00%) 0 |
| Syncope subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 3 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Tympanic membrane perforation subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Gastrointestinal disorders Abdominal Pain subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 2 / 14 (14.29%) 3 | 0 / 14 (0.00%) 0 |
| Abdominal Pain upper subjects affected / exposed occurrences (all) | 2 / 15 (13.33%) 3 | 1 / 14 (7.14%) 1 | 1 / 14 (7.14%) 1 |
| Constipation subjects affected / exposed occurrences (all) | 2 / 15 (13.33%) 2 | 1 / 14 (7.14%) 1 | 1 / 14 (7.14%) 1 |
| Diarrhoea subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 14 (0.00%) 0 | 1 / 14 (7.14%) 1 |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 3 / 14 (21.43%) 4 |
| Mouth Ulceration subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Toothache | | | |

| | | | |
|--|----------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Diarrhoea haemorrhagic subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 14 (7.14%) 1 | 0 / 14 (0.00%) 0 |
| Flatulence subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Hepatobiliary disorders Hepatomegaly subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 14 (7.14%) 1 | 0 / 14 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Hypertrichosis subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 14 (0.00%) 0 | 1 / 14 (7.14%) 1 |
| Rash subjects affected / exposed occurrences (all) | 2 / 15 (13.33%) 2 | 1 / 14 (7.14%) 1 | 2 / 14 (14.29%) 3 |
| Eczema subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 14 (7.14%) 1 |
| Perioral dermatitis subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Pruritis subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Dry skin subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Erythema subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 14 (7.14%) 1 | 0 / 14 (0.00%) 0 |
| Rash macropapular | | | |

| | | | |
|--|----------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Urticaria subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 14 (7.14%) 2 |
| Viral rash subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Renal and urinary disorders Chromaturia subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Proteinuria subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 14 (7.14%) 1 |
| Endocrine disorders Cushingoid subjects affected / exposed occurrences (all) | 4 / 15 (26.67%) 4 | 1 / 14 (7.14%) 1 | 1 / 14 (7.14%) 1 |
| Growth hormone deficiency subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 14 (7.14%) 1 |
| Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all) | 4 / 15 (26.67%) 4 | 2 / 14 (14.29%) 2 | 0 / 14 (0.00%) 0 |
| Back pain subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 14 (0.00%) 0 | 1 / 14 (7.14%) 1 |
| Athralgia subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Muscle spasms subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 14 (7.14%) 1 |
| Myalgia | | | |

| | | | |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 0 | 2 |
| Costrochondritis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 0 | 1 |
| Joint contracture | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 0 | 1 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscle atrophy | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 14 (7.14%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 14 (7.14%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 14 (7.14%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vertebral wedging | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Agitation | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 14 (7.14%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 1 | 1 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 15 (13.33%) | 1 / 14 (7.14%) | 2 / 14 (14.29%) |
| occurrences (all) | 8 | 2 | 5 |

| | | | |
|---|----------------------|----------------------|----------------------|
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 3 / 15 (20.00%) 7 | 3 / 14 (21.43%) 6 | 2 / 14 (14.29%) 5 |
| Rhinitis subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 2 / 14 (14.29%) 3 |
| Enterobiasis subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Conjunctivitis subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 14 (7.14%) 1 |
| Ear Infection subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 2 | 1 / 14 (7.14%) 1 | 1 / 14 (7.14%) 2 |
| Gastroenteritis subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 14 (7.14%) 1 | 1 / 14 (7.14%) 1 |
| Tonsillitis subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 2 / 14 (14.29%) 2 | 0 / 14 (0.00%) 0 |
| Viral Infection subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 14 (7.14%) 1 | 0 / 14 (0.00%) 0 |
| COVID-19 subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 14 (0.00%) 0 | 1 / 14 (7.14%) 1 |
| Cystitis subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Fungal Infection subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 14 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Gastroenteritis viral/viral gastroenteritis | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hand-foot-and-mouth disease | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 0 | 1 |
| Impetigo | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 2 / 14 (14.29%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Moluscum contagiosum | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 0 | 1 |
| Otitis media bacterial | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 14 (7.14%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 0 | 1 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 14 (7.14%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory track infection viral | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Streptococcal infection | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Metabolism and nutrition disorders | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| Increased appetite | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 1 / 14 (7.14%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Vitamin D Deficiency | | | |
| subjects affected / exposed | 2 / 15 (13.33%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Overweight | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Polydipsia | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 14 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 04 May 2018 | <ol style="list-style-type: none">1. To update blood volumes collected for clinical laboratory testing and PD biomarker evaluation;2. To clarify that the blood and urine samples collected at the Screening Visit for clinical laboratory testing do not need to be collected after the subject has fasted;3. To clarify that vamorolone should be used with caution with any drug metabolized by CYP3A4;4. To clarify storage and use of blood samples for future exploratory research studies;5. To remove administration of the Ease of Study Medication Administration Assessment from Day 1 Visit assessments;6. To change the region imaged by spine x-ray from T4-L4 to T4-L5;7. To clarify endpoints and revise the statistical methodology;8. To clarify the definition of time windows around study visits;9. To clarify that fractures reported during the Screening Period using the Fracture Questionnaire will be recorded as Medical History;10. To change the name of the Synacthen Test to the ACTH Stimulation Test and to clarify that Cosyntropin (also known as tetracosactide) is administered to stimulate cortisol response;11. To clarify that the ACTH Stimulation Test will include insertion of a saline lock;12. To clarify that ACTH Stimulation testing should be initiated as close to 8 AM local time as possible, and that the time 0 blood sample for cortisol measurement should be collected immediately prior to Cosyntropin administration;13. To change the name of the Extremity Fracture Questionnaire to Fracture Questionnaire to more accurately reflect the nature of the fractures (vertebral and non-vertebral) to be collected;14. To revise the definition of protocol deviation/violation;15. To clarify that GLP studies were conducted in, or inspected by, a country that has implemented the Organisation for Economic Cooperation and Development (OECD) Mutual Acceptance of Data (MAD) system;16. To update Section 1.5 Overall Benefit/Risk with clinical data;17. To update version of the Investigator's Brochure re |
| 05 March 2019 | <ol style="list-style-type: none">1. To correct contact information for the Medical Monitor;2. To update Section 1.3 Clinical Experience with results from the VBP15-002 and VBP15-003 clinical trials in DMD boys;3. To update Section 1.5 Overall Benefit/Risk;4. To revise exclusion criterion #7 regarding prior use of glucocorticoids;5. To add an exclusion criterion excluding use of live attenuated vaccines within 14 days prior to first dose of study medication;6. To exclude subjects who have siblings currently enrolled in, or intending to enroll in during the subject's participation in this study, any vamorolone study or Expanded Access Program;7. To delete use of the Child Behavior Checklist behavioral assessment tool;8. To clarify that the PARS III assessment tool is a measure of behavior/neuropsychology, and the PODCI is a measure of physical functioning;9. To specify that the PODCI results will be analyzed for vamorolone vs. placebo, and the PARS III results will be analyzed for vamorolone vs. prednisone;17. To clarify that subjects who opt to continue treatment with vamorolone at study completion may be given access to vamorolone through an additional vamorolone study or general access program;18. To remove the responsibility of the DSMB to review accumulating study efficacy data, in response to FDA feedback;19. To clarify the circumstances under which additional subjects may be enrolled;20. To clarify that an email with each subject randomization number will not be sent to the site investigator at the time of randomization;21. To clarify the blinding status following the Week 24 analyses;22. To add sensitivity analyses for missing data;23. To add the 6MWT (comparison of vamorolone vs. prednisone) to the sequential testing procedure for the secondary efficacy endpoints;24. To specify that statistical analyses will be performed using SAS® version 9.4 or later;25. To define time windows around scheduled study visits;26. To update the Schedule of Study Activities to clarify |

| | |
|----------------|--|
| 21 May 2019 | <ol style="list-style-type: none"> 1. To revise Inclusion Criterion #7 to clarify that subjects with abnormal and clinically-significant vitamin D levels will not be excluded from randomization; 2. To revise Inclusion Criterion #8 to allow subjects who have had 2 doses of varicella vaccine prior to randomization, with or without serologic evidence of immunity, to be eligible for randomization to treatment; 3. To revise Sections 6.1 and 7.2.5 to reflect that varicella immunity may be demonstrated by a positive anti-varicella antibody titer or documentation of 2 doses of varicella vaccine; 4. To revise Section 5.6 to clarify instructions for study drug dose interruption; and 5. To correct typographical error in the Synopsis, Exclusion Criterion #7 to make consistent with Section 4.3, Exclusion Criterion #7. |
| 28 August 2020 | <ol style="list-style-type: none"> 1. To revise one of the primary objectives of the study to compare the efficacy of vamorolone administered orally at a dose of 6.0 mg/kg/day vs. placebo over a 24-week treatment period; 2. To revise the primary efficacy endpoint to TTSTAND velocity, comparison of vamorolone 6.0 mg/kg/day vs. placebo in change from baseline to Week 24, to align with the primary objective; 3. To add an additional secondary objective of the study to compare the efficacy of vamorolone administered orally at a dose of 2.0 mg/kg/day vs. placebo over a 24-week treatment period; 4. To delete a secondary objective of the study comparing the efficacy of vamorolone 2.0 mg/kg/day vs. 6.0 mg/kg/day over 24 weeks; 5. To revise the list of safety endpoints to include linear growth velocity, and to clarify the endpoints for BMI z-score and ACTH Stimulation Test; 6. To revise the secondary efficacy endpoints for Treatment Period #1; 7. To add exploratory efficacy endpoints for Treatment Period #1; 8. To add comparison of each vamorolone group to the placebo group for PARS III; 9. To clarify Ease of Study Drug Administration exploratory endpoint; 10. To revise the methodology for sample size calculation, in consideration of the revised primary efficacy endpoint; 11. To add a Per Protocol Population for statistical analyses; 12. To revise the multiple testing procedures for the efficacy endpoints; 13. To revise the statistical methodology for efficacy and safety analyses; 14. To clarify the circumstances under which hospitalizations should be considered serious adverse events; 15. To add assessment of suicidality and abuse potential associated with treatment from examination of adverse event data; 16. To clarify that demographic and baseline characteristics summary tables will not be presented by age stratification; |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported