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)	EMEA-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	5.40	5.42	
full range (min-max)	4.1 to 7.0	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 (± 0.0628)	0.054 (± 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 gasteroenteritis			
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 gasteroenteritis			
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	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Peripheral coldness			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	7 / 28 (25.00%)	3 / 28 (10.71%)	3 / 15 (20.00%)
occurrences (all)	8	3	5
Asthenia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	2
Impaired healing			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Thirst			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 28 (17.86%)	3 / 28 (10.71%)	2 / 15 (13.33%)
occurrences (all)	8	3	2
Nasal congestion			

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 postive			

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	1 / 28 (3.57%)	1 / 28 (3.57%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Back injury			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Vaccination complication			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 28 (10.71%)	2 / 28 (7.14%)	1 / 15 (6.67%)
occurrences (all)	3	2	1
Psychomotor hyperactivity			
subjects affected / exposed	2 / 28 (7.14%)	0 / 28 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
Dizziness			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Poor quality sleep			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Seizure			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	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
Flatulance			
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	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Hypertrichosis			
subjects affected / exposed	1 / 28 (3.57%)	3 / 28 (10.71%)	1 / 15 (6.67%)
occurrences (all)	1	3	1
Rash			
subjects affected / exposed	2 / 28 (7.14%)	2 / 28 (7.14%)	2 / 15 (13.33%)
occurrences (all)	2	2	2
Eczema			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Perioral dermatitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Pruritis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Dry skin			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Rash macropapular			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Viral rash			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			

Chromaturia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Proteinuria			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	4 / 28 (14.29%)	9 / 28 (32.14%)	4 / 15 (26.67%)
occurrences (all)	4	9	4
Growth hormone deficiency			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	2 / 28 (7.14%)	3 / 28 (10.71%)	4 / 15 (26.67%)
occurrences (all)	2	3	5
Back pain			
subjects affected / exposed	1 / 28 (3.57%)	2 / 28 (7.14%)	0 / 15 (0.00%)
occurrences (all)	1	3	0
Athralgia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 28 (3.57%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
Muscle spasms			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Myalgia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Costrochondritis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Joint contracture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	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			
Gasteroenteritis			
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
Tonsilitis			
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 gasteroenteritis			
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
Steptococcal 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	3 / 15 (20.00%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
Weight increased			
subjects affected / exposed	1 / 15 (6.67%)	1 / 14 (7.14%)	1 / 14 (7.14%)
occurrences (all)	1	1	1
Cortisol decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Bacterial test postive			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Blood pressure increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Blood triglycerides increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram abnormal			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Glycosylated haemoglobin increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Lipase decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Urine analysis abnormal			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	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	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
Tympanic membrane perforation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 15 (6.67%)	2 / 14 (14.29%)	0 / 14 (0.00%)
occurrences (all)	1	3	0
Abdominal Pain upper			
subjects affected / exposed	2 / 15 (13.33%)	1 / 14 (7.14%)	1 / 14 (7.14%)
occurrences (all)	3	1	1
Constipation			
subjects affected / exposed	2 / 15 (13.33%)	1 / 14 (7.14%)	1 / 14 (7.14%)
occurrences (all)	2	1	1
Diarrhoea			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	3 / 14 (21.43%)
occurrences (all)	0	0	4
Mouth Ulceration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Toothache			

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

subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	2
Viral rash			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Proteinuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Endocrine disorders			
Cushingoid			
subjects affected / exposed	4 / 15 (26.67%)	1 / 14 (7.14%)	1 / 14 (7.14%)
occurrences (all)	4	1	1
Growth hormone deficiency			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	4 / 15 (26.67%)	2 / 14 (14.29%)	0 / 14 (0.00%)
occurrences (all)	4	2	0
Back pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Athralgia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	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			
Gasteroenteritis			
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	3 / 15 (20.00%)	3 / 14 (21.43%)	2 / 14 (14.29%)
occurrences (all)	7	6	5
Rhinitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	3
Enterobiasis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Ear Infection			
subjects affected / exposed	1 / 15 (6.67%)	1 / 14 (7.14%)	1 / 14 (7.14%)
occurrences (all)	2	1	2
Gastroenteritis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Tonsilitis			
subjects affected / exposed	0 / 15 (0.00%)	2 / 14 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Viral Infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
COVID-19			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Cystitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Fungal Infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral/viral gasteroenteritis			

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
Steptococcal 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	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	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	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	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