Clinical trial results:
A 24-month Phase II Open-label, Multicenter Long-term Extension Study to Assess the Long-term Safety and Efficacy of Vamorolone in Boys with Duchenne Muscular Dystrophy (DMD)

Summary

EudraCT number	2017-003568-10
Trial protocol	SE GB
Global end of trial date	27 October 2021

Results information

Result version number	v1 (current)
This version publication date	11 May 2022
First version publication date	11 May 2022

Trial information

Trial identification

Sponsor protocol code	VBP15-LTE

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03038399
WHO universal trial number (UTN)	-

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	27 October 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of vamorolone, administered orally at daily doses up to 6.0 mg/kg over a 24-month Treatment Period, in young boys with DMD who completed protocol VBP15-003;

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	02 February 2017
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	Sweden: 4
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	United States: 18
Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	Israel: 5
Worldwide total number of subjects	46
EEA total number of subjects	4

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)	46
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:

Only those who have participated in the VBP15-003 trial are able to participate in the VBP15-LTE trial

Pre-assignment

Screening details:

Subject has previously completed study VBP15-003 up to and including the Week 24 Final assessments, prior to enrolling in the VBP15-LTE study at the conclusion of the VBP15-003 Week 24 Visit [Note: if entering the dose-tapering period, subject is enrolling within 8 weeks after the VBP15-003 final visit following dose-tapering.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Dose Level Group 1

Arm description:

Participants enrolled in Dose Level Group 1 will receive vamorolone 0.25 mg/kg/day

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

Dosage and administration details:

4% wt/wt oral suspension; administered daily

Arm title	Dose Level Group 2

Arm description:

Participants enrolled in Dose Level Group 2 will receive vamorolone 0.75 mg/kg/day

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

Dosage and administration details:

4% wt/wt oral suspension; administered daily

Arm title	Dose Level Group 3

Arm description:

Participants enrolled in Dose Level Group 3 will receive vamorolone 2.0 mg/kg/day

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

Dosage and administration details:
4% wt/wt oral suspension; administered daily

Arm title	Dose Level Group 4

Arm description:
Participants enrolled in Dose Level Group 4 will receive vamorolone 6.0 mg/kg/day

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

Dosage and administration details:
4% wt/wt oral suspension; administered daily

Number of subjects in period 1	Dose Level Group 1	Dose Level Group 2	Dose Level Group 3
Started	11	12	12
Completed	11	12	12

Number of subjects in period 1	Dose Level Group 4
Started	11
Completed	11

Period 2

Period 2 title	Treatment Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Dose Level Group 1

Arm description:
Participants enrolled in Dose Level Group 1 will receive vamorolone 0.25 mg/kg/day

Arm type	Experimental

Investigational medicinal product name	Vamorolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

4% wt/wt oral suspension; administered daily

Arm title	Dose Level Group 2

Arm description:

Participants enrolled in Dose Level Group 2 will receive vamorolone 0.75 mg/kg/day

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

Dosage and administration details:

4% wt/wt oral suspension; administered daily

Arm title	Dose Level Group 3

Arm description:

Participants enrolled in Dose Level Group 3 will receive vamorolone 2.0 mg/kg/day

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

Dosage and administration details:

4% wt/wt oral suspension; administered daily

Arm title	Dose Level Group 4

Arm description:

Participants enrolled in Dose Level Group 4 will receive vamorolone 6.0 mg/kg/day

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

Dosage and administration details:

4% wt/wt oral suspension; administered daily

Number of subjects in period 2[1]	Dose Level Group 1	Dose Level Group 2	Dose Level Group 3
Started	11	12	12
Completed	0	0	11
Not completed	11	23	27
Desire to be eligible for other clinical trials	-	-	-

Transferred to other arm/group	11	23	27
undue study burden	-	-	-
loss of muscle strength	-	-	-
Joined	0	11	26
Transferred in from other group/arm	-	11	26

Number of subjects in period 2[1]	Dose Level Group 4
Started	11
Completed	32
Not completed	9
Desire to be eligible for other clinical trials	3
Transferred to other arm/group	4
undue study burden	1
loss of muscle strength	1
Joined	30
Transferred in from other group/arm	30

Notes:

[1] - The number of subjects transferring in and out of the arms in the period are not the same. It is expected the net number of transfers in and out of the arms in a period, will be zero.
Justification: subjects were allowed to escalate and de-escalate dose levels throughout the trial

Baseline characteristics

Reporting groups	
Reporting group title	Dose Level Group 1
Reporting group description:	
Participants enrolled in Dose Level Group 1 will receive vamorolone 0.25 mg/kg/day	
Reporting group title	Dose Level Group 2
Reporting group description:	
Participants enrolled in Dose Level Group 2 will receive vamorolone 0.75 mg/kg/day	
Reporting group title	Dose Level Group 3
Reporting group description:	
Participants enrolled in Dose Level Group 3 will receive vamorolone 2.0 mg/kg/day	
Reporting group title	Dose Level Group 4
Reporting group description:	
Participants enrolled in Dose Level Group 4 will receive vamorolone 6.0 mg/kg/day	

Reporting group values	Dose Level Group 1	Dose Level Group 2	Dose Level Group 3
Number of subjects	11	12	12
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)	11	12	12
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
Gender categorical Units: Subjects			
Female	0	0	0
Male	11	12	12

Reporting group values	Dose Level Group 4	Total	
Number of subjects	11	46	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	11	46	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	

85 years and over	0	0	

Gender categorical Units: Subjects			
Female	0	0	
Male	11	46	

End points

End points reporting groups

Reporting group title	Dose Level Group 1
Reporting group description:	
Participants enrolled in Dose Level Group 1 will receive vamorolone 0.25 mg/kg/day	
Reporting group title	Dose Level Group 2
Reporting group description:	
Participants enrolled in Dose Level Group 2 will receive vamorolone 0.75 mg/kg/day	
Reporting group title	Dose Level Group 3
Reporting group description:	
Participants enrolled in Dose Level Group 3 will receive vamorolone 2.0 mg/kg/day	
Reporting group title	Dose Level Group 4
Reporting group description:	
Participants enrolled in Dose Level Group 4 will receive vamorolone 6.0 mg/kg/day	
Reporting group title	Dose Level Group 1
Reporting group description:	
Participants enrolled in Dose Level Group 1 will receive vamorolone 0.25 mg/kg/day	
Reporting group title	Dose Level Group 2
Reporting group description:	
Participants enrolled in Dose Level Group 2 will receive vamorolone 0.75 mg/kg/day	
Reporting group title	Dose Level Group 3
Reporting group description:	
Participants enrolled in Dose Level Group 3 will receive vamorolone 2.0 mg/kg/day	
Reporting group title	Dose Level Group 4
Reporting group description:	
Participants enrolled in Dose Level Group 4 will receive vamorolone 6.0 mg/kg/day	

Primary: Number of Participants With Treatment-related Adverse Events as Assessed by CTCAE Version 4.03

End point title	Number of Participants With Treatment-related Adverse Events as Assessed by CTCAE Version 4.03[1]
End point description:	
To evaluate the long-term safety and tolerability of vamorolone, administered orally at daily doses up to 6.0 mg/kg/day over a 24- month Treatment Period, in boys ages 4-7 years with DMD; Treatment-emergent adverse events (TEAEs) are defined as any adverse event or worsening of an existing conditions after initiation of the investigational product and through the subject's last study visit (study completion or early termination);	
End point type	Primary
End point timeframe:	
24 months	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: no statistical analysis

End point values	Dose Level Group 1	Dose Level Group 2	Dose Level Group 3	Dose Level Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	23	38	41
Units: subjects	4	14	29	39

Statistical analyses

No statistical analyses for this end point

Primary: Total Number of Adverse Events as Assessed by CTCAE Version 4.03

End point title	Total Number of Adverse Events as Assessed by CTCAE Version 4.03[2]

End point description:

To evaluate the long-term safety and tolerability of vamorolone, administered orally at daily doses up to 6.0 mg/kg/day over a 24-month Treatment Period, in boys ages 4-7 years with DMD. Treatment-emergent adverse events (TEAEs) are defined as any adverse event or worsening of an existing conditions after initiation of the investigational product and through the subject's last study visit (study completion or early termination).

End point type	Primary

End point timeframe:

24 months

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: no statistical analysis

End point values	Dose Level Group 1	Dose Level Group 2	Dose Level Group 3	Dose Level Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	23	38	41
Units: events	14	34	202	300

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

24 months

Adverse event reporting additional description:

Adverse events, including Serious Adverse Events (SAEs will be assessed at each study visit and recorded throughout the 24 months treatment period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Dose Level Group 1
Reporting group description: -	
Reporting group title	Dose Level Group 2
Reporting group description: -	
Reporting group title	Dose Level Group 3
Reporting group description: -	
Reporting group title	Dose Level Group 4
Reporting group description: -	

Serious adverse events	Dose Level Group 1	Dose Level Group 2	Dose Level Group 3
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	1 / 23 (4.35%)	0 / 38 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Renal and urinary disorders			
Myoglobinuria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 23 (0.00%)	0 / 38 (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			
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 23 (4.35%)	0 / 38 (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	Dose Level Group 4		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 41 (2.44%)		

number of deaths (all causes) number of deaths resulting from adverse events	0		
Renal and urinary disorders Myoglobinuria subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 41 (2.44%) 0 / 1 0 / 0		
Infections and infestations Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 41 (0.00%) 0 / 0 0 / 0		

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

Non-serious adverse events	Dose Level Group 1	Dose Level Group 2	Dose Level Group 3
Total subjects affected by non-serious adverse events subjects affected / exposed	 4 / 11 (36.36%)	 14 / 23 (60.87%)	 29 / 38 (76.32%)
Investigations Weight increased subjects affected / exposed occurrences (all) Blood triglycerides increased subjects affected / exposed occurrences (all)	 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0	 0 / 23 (0.00%) 0 0 / 23 (0.00%) 0	 2 / 38 (5.26%) 2 0 / 38 (0.00%) 0
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all) Joint injury subjects affected / exposed occurrences (all) Limb injury subjects affected / exposed occurrences (all) Arthropod bite	 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 	 1 / 23 (4.35%) 1 0 / 23 (0.00%) 0 0 / 23 (0.00%) 0 	 4 / 38 (10.53%) 4 2 / 38 (5.26%) 2 3 / 38 (7.89%) 3

subjects affected / exposed	1 / 11 (9.09%)	1 / 23 (4.35%)	1 / 38 (2.63%)
occurrences (all)	1	1	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 11 (0.00%)	0 / 23 (0.00%)	4 / 38 (10.53%)
occurrences (all)	0	0	4
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 23 (4.35%)	1 / 38 (2.63%)
occurrences (all)	0	1	1
Influenza like illness			
subjects affected / exposed	0 / 11 (0.00%)	1 / 23 (4.35%)	0 / 38 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 23 (0.00%)	9 / 38 (23.68%)
occurrences (all)	0	0	9
Upper respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	2 / 23 (8.70%)	5 / 38 (13.16%)
occurrences (all)	0	2	5
Medical device site joint pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 23 (0.00%)	0 / 38 (0.00%)
occurrences (all)	1	0	0
Medical device site rash			
subjects affected / exposed	1 / 11 (9.09%)	0 / 23 (0.00%)	0 / 38 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 23 (0.00%)	5 / 38 (13.16%)
occurrences (all)	0	0	5
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 11 (9.09%)	0 / 23 (0.00%)	2 / 38 (5.26%)
occurrences (all)	1	0	2
Gastrointestinal disorders			
Abdominal Pain			

subjects affected / exposed	0 / 11 (0.00%)	0 / 23 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 11 (0.00%)	0 / 23 (0.00%)	1 / 38 (2.63%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 23 (0.00%)	3 / 38 (7.89%)
occurrences (all)	0	0	3
Diarrhoea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 23 (4.35%)	1 / 38 (2.63%)
occurrences (all)	0	1	1
Vomiting			
subjects affected / exposed	1 / 11 (9.09%)	0 / 23 (0.00%)	5 / 38 (13.16%)
occurrences (all)	1	0	5
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 11 (9.09%)	1 / 23 (4.35%)	7 / 38 (18.42%)
occurrences (all)	1	1	7
Oropharyngeal pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 23 (4.35%)	1 / 38 (2.63%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 11 (0.00%)	2 / 23 (8.70%)	0 / 38 (0.00%)
occurrences (all)	0	2	0
Urticaria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 23 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Aggression			
subjects affected / exposed	1 / 11 (9.09%)	0 / 23 (0.00%)	0 / 38 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	1 / 11 (9.09%)	0 / 23 (0.00%)	0 / 38 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			

Muscle spasms			
subjects affected / exposed	0 / 11 (0.00%)	0 / 23 (0.00%)	1 / 38 (2.63%)
occurrences (all)	0	0	1
Osteopenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 23 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 11 (0.00%)	3 / 23 (13.04%)	5 / 38 (13.16%)
occurrences (all)	0	3	5
Back pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 23 (0.00%)	2 / 38 (5.26%)
occurrences (all)	0	0	2
Infections and infestations			
Ear Infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 23 (4.35%)	2 / 38 (5.26%)
occurrences (all)	0	1	2
Gastroenteritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 23 (0.00%)	3 / 38 (7.89%)
occurrences (all)	0	0	3
Influenza			
subjects affected / exposed	0 / 11 (0.00%)	1 / 23 (4.35%)	3 / 38 (7.89%)
occurrences (all)	0	1	3
Nasopharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 23 (4.35%)	7 / 38 (18.42%)
occurrences (all)	0	1	7
Otitis media			
subjects affected / exposed	0 / 11 (0.00%)	0 / 23 (0.00%)	3 / 38 (7.89%)
occurrences (all)	0	0	3
Pharyngitis streptococcal			
subjects affected / exposed	1 / 11 (9.09%)	2 / 23 (8.70%)	2 / 38 (5.26%)
occurrences (all)	1	2	2
Sinusitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 23 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
Body tinea			

subjects affected / exposed	1 / 11 (9.09%)	0 / 23 (0.00%)	0 / 38 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 23 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 11 (9.09%)	0 / 23 (0.00%)	0 / 38 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Dose Level Group 4		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 41 (95.12%)		
Investigations			
Weight increased			
subjects affected / exposed	10 / 41 (24.39%)		
occurrences (all)	10		
Blood triglycerides increased			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	6 / 41 (14.63%)		
occurrences (all)	6		
Joint injury			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences (all)	0		
Limb injury			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences (all)	0		
Arthropod bite			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 41 (17.07%)		
occurrences (all)	7		
General disorders and administration			

site conditions Chest pain subjects affected / exposed occurrences (all) Influenza like illness subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Medical device site joint pain subjects affected / exposed occurrences (all) Medical device site rash subjects affected / exposed occurrences (all)	 3 / 41 (7.32%) 3 3 / 41 (7.32%) 3 8 / 41 (19.51%) 8 6 / 41 (14.63%) 6 0 / 41 (0.00%) 0 0 / 41 (0.00%) 0		
Ear and labyrinth disorders Ear Pain subjects affected / exposed occurrences (all)	 4 / 41 (9.76%) 4		
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	 0 / 41 (0.00%) 0		
Gastrointestinal disorders Abdominal Pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all)	 6 / 41 (14.63%) 6 5 / 41 (12.20%) 5 8 / 41 (19.51%) 8		

Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	3 / 41 (7.32%) 3 7 / 41 (17.07%) 7		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	 8 / 41 (19.51%) 8 3 / 41 (7.32%) 3		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all)	 1 / 41 (2.44%) 1 1 / 41 (2.44%) 1		
Psychiatric disorders Aggression subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all)	 0 / 41 (0.00%) 0 0 / 41 (0.00%) 0		
Musculoskeletal and connective tissue disorders Muscle spasms subjects affected / exposed occurrences (all) Osteopenia subjects affected / exposed occurrences (all) Pain in extremity	 3 / 41 (7.32%) 3 4 / 41 (9.76%) 4 		

subjects affected / exposed	6 / 41 (14.63%)		
occurrences (all)	6		
Back pain			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Infections and infestations			
Ear Infection			
subjects affected / exposed	4 / 41 (9.76%)		
occurrences (all)	4		
Gastroenteritis			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Influenza			
subjects affected / exposed	6 / 41 (14.63%)		
occurrences (all)	6		
Nasopharyngitis			
subjects affected / exposed	12 / 41 (29.27%)		
occurrences (all)	12		
Otitis media			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Pharyngitis streptococcal			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Sinusitis			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences (all)	0		
Body tinea			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences (all)	0		
Gastroenteritis viral			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 October 2018	1. To update Section 1 Introduction with safety results from Phase II studies in DMD boys (VBP15-002 and VBP15-003) 2. To update Section 1.5 Overall Benefit/Risk 3. To update Section 13 References 4. To clarify that dose may be escalated incrementally to 6.0 mg/kg/day 5. To clarify the circumstances under which study drug dose should be interrupted, de-escalated, or discontinued 6. To allow dose de-escalation from 6.0 mg/kg/day to 2.0 mg/kg/day to be followed by dose escalation to 4.0 mg/kg/day,balancing efficacy and safety concerns, in the opinion of the Investigator 7. To prohibit use of Exondys 51, Translarna, and other medications indicated for treatment of DMD during the study 8. To add details of Data and Safety Monitoring Board (DSMB) responsibilities 9. To add collection of 8.5 mL of blood at the Month 24 Visit for deoxyribonucleic acid (DNA) testing for established genetic modifiers of DMD 10. To add spine x-ray for detection of fracture at the Month 24 Visit 11. To add hand x-ray for assessment of bone age at the Month 24 Visit 12. To remove the designation of BMI z-score as the primary safety outcome 13. To update the primary efficacy endpoint 14. To remove comparison of vamorolone with prednisone-treated historical control data for serum PD biomarkers of safety 15. To add comparison of vamorolone to prednisone- and deflazacort-treated historical control data for bone age, spine fracture, and height z-score, and comparison to deflazacort-treated historical control data for BMI z-score 16. To update the statistical methodology and composition of the control populations 17. To clarify that collection of the Pediatric Outcomes Data Collection Instrument (PODCI) does not need to be repeated at the VBP15-LTE Baseline Visit if the Baseline Visit occurs ≤ 28 days after the date of the VBP15-003 Week 24 Visit 18. To clarify the PD biomarkers to be evaluated

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32956407

http://www.ncbi.nlm.nih.gov/pubmed/35076703