



Clinical trial results:

An open-label extension study of the long-term safety, tolerability and efficacy of GSK2402968 in subjects with Duchenne Muscular Dystrophy Summary

EudraCT number	2011-001266-17
Trial protocol	BE FR DE GB NL ES IT Outside EU/EEA BG HU DK CZ
Global end of trial date	18 February 2014

Results information

Result version number	v1 (current)
This version publication date	23 March 2017
First version publication date	23 March 2017

Trial information

Trial identification

Sponsor protocol code	DMD114349
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01480245
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BioMarin Pharmaceutical Inc.
Sponsor organisation address	105 Digital Drive, Novato, United States, CA94949
Public contact	Clinical Trials Information, BioMarin Pharmaceutical Inc., clinicaltrials@bmrn.com
Scientific contact	Clinical Trials Information, BioMarin Pharmaceutical Inc., clinicaltrials@bmrn.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-000746-PIP01-09
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	24 July 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 February 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long term safety, tolerability and efficacy of subcutaneous 6mg/kg/week GSK2402968 in subjects with DMD who have participated in either DMD114117 or DMD114044.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 August 2011
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	Argentina: 6
Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Brazil: 16
Country: Number of subjects enrolled	Bulgaria: 2
Country: Number of subjects enrolled	Canada: 21
Country: Number of subjects enrolled	Chile: 7
Country: Number of subjects enrolled	Czech Republic: 7
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Germany: 29
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Italy: 25
Country: Number of subjects enrolled	Japan: 14
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	Netherlands: 10
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	Russian Federation: 8
Country: Number of subjects enrolled	Spain: 16
Country: Number of subjects enrolled	Taiwan: 3

Country: Number of subjects enrolled	Turkey: 12
Country: Number of subjects enrolled	United Kingdom: 10
Worldwide total number of subjects	233
EEA total number of subjects	132

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)	207
Adolescents (12-17 years)	26
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:

This study will include all eligible subjects who participated in studies DMD114117 or DMD114044, and choose to enter this open label study.

Period 1

Period 1 title	114349 (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	6 mg/kg Drisapersen Continuous

Arm description:

6 mg/kg Drisapersen Continuous

Arm type	Experimental
Investigational medicinal product name	drisapersen
Investigational medicinal product code	BMN-051
Other name	PRO-051, GSK2402968
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Eligible subjects will receive drisapersen 6mg/kg/weekly.

Drisapersen will be supplied as 3 ml vials containing 1ml or 0.7ml sterile solution for subcutaneous injection. The strength of drisapersen solution will be 200 mg/ml.

Arm title	6 mg/kg Drisapersen Intermittent
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Arm description:

6 mg/kg Drisapersen Intermittent

Arm type	Experimental
Investigational medicinal product name	drisapersen
Investigational medicinal product code	BMN-051
Other name	PRO-051, GSK2402968
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Eligible subjects will receive drisapersen 6mg/kg/week for 8 weeks followed by 4 weeks off of drug.

Drisapersen will be supplied as 3 ml vials containing 1ml or 0.7ml sterile solution for subcutaneous injection. The strength of drisapersen solution will be 200 mg/ml.

Arm title	Natural History
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Arm description:

Natural History

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	6 mg/kg Drisapersen Continuous	6 mg/kg Drisapersen Intermittent	Natural History
Started	228	12	17
Completed	0	0	0
Not completed	228	12	17
Consent withdrawn by subject	9	-	1
Adverse event	1	-	-
Study Terminated by Sponsor	216	12	15
Lack of efficacy	2	-	1

Baseline characteristics

Reporting groups

Reporting group title	6 mg/kg Drisapersen Continuous
Reporting group description:	
6 mg/kg Drisapersen Continuous	
Reporting group title	6 mg/kg Drisapersen Intermittent
Reporting group description:	
6 mg/kg Drisapersen Intermittent	
Reporting group title	Natural History
Reporting group description:	
Natural History	

Reporting group values	6 mg/kg Drisapersen Continuous	6 mg/kg Drisapersen Intermittent	Natural History
Number of subjects	228	12	17
Age categorical			
Units: Subjects			
0-85 years and over	228	12	17
Age continuous			
Units: Years			
arithmetic mean	8.9	9.9	8.7
standard deviation	± 2.12	± 1.73	± 1.69
Gender categorical			
Units: Subjects			
Female	0	0	0
Male	228	12	17

Reporting group values	Total		
Number of subjects	233		
Age categorical			
Units: Subjects			
0-85 years and over	233		
Age continuous			
Units: Years			
arithmetic mean	-		
standard deviation			
Gender categorical			
Units: Subjects			
Female	0		
Male	233		

End points

End points reporting groups

Reporting group title	6 mg/kg Drisapersen Continuous
Reporting group description:	6 mg/kg Drisapersen Continuous
Reporting group title	6 mg/kg Drisapersen Intermittent
Reporting group description:	6 mg/kg Drisapersen Intermittent
Reporting group title	Natural History
Reporting group description:	Natural History

Primary: change from baseline in muscle function using the 6MWD at week 104

End point title	change from baseline in muscle function using the 6MWD at week 104 ^[1]
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End point description:

The primary efficacy endpoint for this study was the difference between baseline and Week 104 in 6MWD for subjects on the continuous drisapersen treatment group for the Modified Ambulant ITT population. However, only 4 subjects in the continuous drisapersen group and 1 subject in the natural history arm had efficacy data at Week 104. Therefore, the efficacy results presented in this section focus on data up through Week 72.

End point type	Primary
End point timeframe:	Week 72

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: Study has been terminated early and no full SAP has been used.

End point values	6 mg/kg Drisapersen Continuous	6 mg/kg Drisapersen Intermittent	Natural History	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	3	2	
Units: Meter				
arithmetic mean (standard deviation)	-90.81 (± 99.732)	-88.57 (± 115.366)	-41 (± 137.179)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Study Period

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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Reporting groups

Reporting group title	6 mg/kg Drisapersen Continuous
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Reporting group description: -

Reporting group title	Natural History
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Reporting group description: -

Reporting group title	6 mg/kg Drisapersen Intermittent
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Reporting group description: -

Serious adverse events	6 mg/kg Drisapersen Continuous	Natural History	6 mg/kg Drisapersen Intermittent
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 228 (11.84%)	0 / 17 (0.00%)	0 / 12 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
International normalised ratio increased			
subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			

subjects affected / exposed	3 / 228 (1.32%)	0 / 17 (0.00%)	0 / 12 (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
Tibia fracture			
subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cyanosis			
subjects affected / exposed	2 / 228 (0.88%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hypotonia			
subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Haemolytic anaemia			
subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	8 / 228 (3.51%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	7 / 8	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Injection site oedema			
subjects affected / exposed	2 / 228 (0.88%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			

subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Optic disc disorder			
subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Proteinuria			

subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	2 / 228 (0.88%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	6 mg/kg Drisapersen Continuous	Natural History	6 mg/kg Drisapersen Intermittent
Total subjects affected by non-serious adverse events			
subjects affected / exposed	208 / 228 (91.23%)	6 / 17 (35.29%)	9 / 12 (75.00%)
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	6 / 228 (2.63%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	7	0	1
Complement factor C3 decreased			
subjects affected / exposed	12 / 228 (5.26%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	16	0	0

Cystatin C increased subjects affected / exposed occurrences (all)	16 / 228 (7.02%) 33	0 / 17 (0.00%) 0	0 / 12 (0.00%) 0
Fibrin D dimer increased subjects affected / exposed occurrences (all)	5 / 228 (2.19%) 6	1 / 17 (5.88%) 1	0 / 12 (0.00%) 0
International normalised ratio increased subjects affected / exposed occurrences (all)	7 / 228 (3.07%) 11	0 / 17 (0.00%) 0	1 / 12 (8.33%) 1
Protein urine present subjects affected / exposed occurrences (all)	30 / 228 (13.16%) 115	0 / 17 (0.00%) 0	0 / 12 (0.00%) 0
Red blood cells urine subjects affected / exposed occurrences (all)	16 / 228 (7.02%) 37	0 / 17 (0.00%) 0	0 / 12 (0.00%) 0
Red blood cells urine positive subjects affected / exposed occurrences (all)	25 / 228 (10.96%) 53	0 / 17 (0.00%) 0	0 / 12 (0.00%) 0
Urine analysis abnormal subjects affected / exposed occurrences (all)	1 / 228 (0.44%) 3	0 / 17 (0.00%) 0	1 / 12 (8.33%) 2
Urine protein/creatinine ratio increased subjects affected / exposed occurrences (all)	20 / 228 (8.77%) 40	0 / 17 (0.00%) 0	0 / 12 (0.00%) 0
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	22 / 228 (9.65%) 35	1 / 17 (5.88%) 1	0 / 12 (0.00%) 0
Fall subjects affected / exposed occurrences (all)	51 / 228 (22.37%) 134	0 / 17 (0.00%) 0	0 / 12 (0.00%) 0
Femur fracture subjects affected / exposed occurrences (all)	1 / 228 (0.44%) 1	0 / 17 (0.00%) 0	1 / 12 (8.33%) 1
Injection related reaction			

subjects affected / exposed	8 / 228 (3.51%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	9	0	1
Ligament sprain			
subjects affected / exposed	13 / 228 (5.70%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	18	1	0
Nervous system disorders			
Aphonia			
subjects affected / exposed	0 / 228 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Burning sensation			
subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Headache			
subjects affected / exposed	63 / 228 (27.63%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	230	0	4
Sensory disturbance			
subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	15 / 228 (6.58%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	21	0	0
Hyperthermia			
subjects affected / exposed	0 / 228 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Injection site atrophy			
subjects affected / exposed	24 / 228 (10.53%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	38	0	2
Injection site bruising			
subjects affected / exposed	19 / 228 (8.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	132	0	0
Injection site discolouration			
subjects affected / exposed	85 / 228 (37.28%)	0 / 17 (0.00%)	2 / 12 (16.67%)
occurrences (all)	307	0	6
Injection site erythema			

subjects affected / exposed	73 / 228 (32.02%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	346	0	4
Injection site haematoma			
subjects affected / exposed	17 / 228 (7.46%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	38	0	3
Injection site haemorrhage			
subjects affected / exposed	3 / 228 (1.32%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	5	0	1
Injection site induration			
subjects affected / exposed	55 / 228 (24.12%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	149	1	1
Injection site pain			
subjects affected / exposed	23 / 228 (10.09%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	81	0	1
Injection site pruritus			
subjects affected / exposed	22 / 228 (9.65%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	47	0	1
Injection site reaction			
subjects affected / exposed	29 / 228 (12.72%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	145	0	0
Injection site swelling			
subjects affected / exposed	17 / 228 (7.46%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	25	0	0
Pyrexia			
subjects affected / exposed	49 / 228 (21.49%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	86	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	31 / 228 (13.60%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	74	1	1
Abdominal pain upper			
subjects affected / exposed	18 / 228 (7.89%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	27	0	1
Diarrhoea			
subjects affected / exposed	43 / 228 (18.86%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	96	0	1

Flatulence			
subjects affected / exposed	1 / 228 (0.44%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	14 / 228 (6.14%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	19	0	0
Toothache			
subjects affected / exposed	2 / 228 (0.88%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	6	1	0
Vomiting			
subjects affected / exposed	59 / 228 (25.88%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	118	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	34 / 228 (14.91%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	40	0	0
Epistaxis			
subjects affected / exposed	24 / 228 (10.53%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	36	1	1
Oropharyngeal pain			
subjects affected / exposed	16 / 228 (7.02%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	23	0	0
Skin and subcutaneous tissue disorders			
Macule			
subjects affected / exposed	0 / 228 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Miliaria			
subjects affected / exposed	0 / 228 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	13 / 228 (5.70%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	23	0	0
Renal and urinary disorders			
Albuminuria			
subjects affected / exposed	3 / 228 (1.32%)	0 / 17 (0.00%)	2 / 12 (16.67%)
occurrences (all)	4	0	2

Haematuria			
subjects affected / exposed	25 / 228 (10.96%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	63	0	3
Proteinuria			
subjects affected / exposed	75 / 228 (32.89%)	0 / 17 (0.00%)	3 / 12 (25.00%)
occurrences (all)	216	0	11
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	19 / 228 (8.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	36	0	0
Pain in extremity			
subjects affected / exposed	30 / 228 (13.16%)	1 / 17 (5.88%)	3 / 12 (25.00%)
occurrences (all)	50	1	3
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	18 / 228 (7.89%)	0 / 17 (0.00%)	2 / 12 (16.67%)
occurrences (all)	21	0	2
Influenza			
subjects affected / exposed	13 / 228 (5.70%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	16	0	0
Nasopharyngitis			
subjects affected / exposed	60 / 228 (26.32%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	116	1	2
Rhinitis			
subjects affected / exposed	20 / 228 (8.77%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	33	1	0
Upper respiratory tract infection			
subjects affected / exposed	26 / 228 (11.40%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	33	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 July 2013	Update to renal criteria timing; update to additional vial fill volume, length of study, removal of all dried bloodspot assessments and analysis, removal of several biomarker tests, minor corrections and clarifications added;
09 October 2013	Instructions for investigators for subject management during the time period while dosing is on hold per drisapersen Dear Investigator Letter

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
09 October 2013	Dosing hold after results of study DMD114044 were analysed. (see amendmends)	-

Notes:

Limitations and caveats

None reported