



## Clinical trial results:

**A phase II, double blind, exploratory, parallel-group, placebo-controlled clinical study to assess two dosing regimens of GSK2402968 for efficacy, safety, tolerability and pharmacokinetics in ambulant subjects with Duchenne muscular dystrophy**

### Summary

EudraCT number	2010-018412-32
Trial protocol	DE BE GB NL FR ES Outside EU/EEA
Global end of trial date	12 September 2012

### Results information

Result version number	v1 (current)
This version publication date	26 October 2019
First version publication date	26 October 2019
Summary attachment (see zip file)	synopsis (dmd114117synopsis.pdf)

### Trial information

#### Trial identification

Sponsor protocol code	DMD114117
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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	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GlaxoSmithKline, GSK Response Centre, 1 8664357343, GSKClinicalSupportHD@GSK.com
Scientific contact	GlaxoSmithKline, GSK Response Centre, 1 8664357343, GSKClinicalSupportHD@GSK.com

Notes:

### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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	29 August 2013
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	12 September 2012
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

•To assess the efficacy of 2 different dosing regimens of subcutaneous drisapersen administered over 24 weeks in ambulant subjects with DMD.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	5 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Turkey: 7
Country: Number of subjects enrolled	United Kingdom: 10
Worldwide total number of subjects	53
EEA total number of subjects	38

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)	53
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:

This study was conducted at 13 study centers in Australia, Belgium, France, Germany, Israel, Netherlands, Spain, Turkey and United Kingdom.

### Pre-assignment

Screening details:

Of the 53 subjects enrolled to study, all the 53 subjects completed the initial six months and the twelve months extension.

### Period 1

Period 1 title	DMD114117 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

The allocation of active and placebo was double-blind. The different injection regimens (continuous or intermittent) were not blinded. This was due to the unacceptable number of additional dummy injections that would have been required to fully blind both regimens.

Blinding was maintained throughout the study for subjects, investigators and any personnel with direct contacts with the sites, until completion of the final assessment for the final subject had been entered onto the database.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Placebo (combined)

Arm description:

Placebo (combined)

Arm type	Placebo
Investigational medicinal product name	Drisapersen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo is supplied as 3 mL vials containing 1 mL sterile solution for subcutaneous injection.

<b>Arm title</b>	6mg/kg Continuous
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Arm description:

6mg/kg Continuous

Arm type	Experimental
Investigational medicinal product name	Drisapersen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Drisapersen is supplied as 3 mL vials containing 1 mL sterile solution for subcutaneous injection. The strength of drisapersen solution was 200 mg/mL.

<b>Arm title</b>	6mg/kg Intermittent
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Arm description:

6mg/kg Intermittent

Arm type	Experimental
Investigational medicinal product name	Drisapersen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Drisapersen is supplied as 3 mL vials containing 1 mL sterile solution for subcutaneous injection. The strength of drisapersen solution was 200 mg/mL.

<b>Number of subjects in period 1</b>	Placebo (combined)	6mg/kg Continuous	6mg/kg Intermittent
Started	18	18	17
Completed	18	18	17

## Baseline characteristics

Reporting groups	
Reporting group title	Placebo (combined)
Reporting group description: Placebo (combined)	
Reporting group title	6mg/kg Continuous
Reporting group description: 6mg/kg Continuous	
Reporting group title	6mg/kg Intermittent
Reporting group description: 6mg/kg Intermittent	

Reporting group values	Placebo (combined)	6mg/kg Continuous	6mg/kg Intermittent
Number of subjects	18	18	17
Age categorical Units: Subjects			
5 - 11	18	18	17
12 - 18	0	0	0
≥ 19	0	0	0
Age continuous Units: Years			
arithmetic mean	6.9	7.2	7.7
standard deviation	± 1.18	± 1.66	± 1.49
Gender categorical Units: Subjects			
Female	0	0	0
Male	18	18	17
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	1
Not Hispanic or Latino	16	17	14
Unknown or Not Reported	2	1	2
Race Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	1	0	0
Native Hawaiian or Other Pacific Islander	1	0	0
Black or African American	0	0	0
White	13	15	14
Other	1	0	0
Unknown or Not Reported	2	3	2
Weight Units: kg			
arithmetic mean	25.03	25.05	28.39
standard deviation	± 5.226	± 7.39	± 9.811
Length Units: cm			

arithmetic mean	118.69	118.42	120.6
standard deviation	± 8.137	± 10.459	± 10.267

Reporting group values	Total		
Number of subjects	53		
Age categorical Units: Subjects			
5 - 11	53		
12 - 18	0		
≥ 19	0		
Age continuous Units: Years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	0		
Male	53		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1		
Not Hispanic or Latino	47		
Unknown or Not Reported	5		
Race Units: Subjects			
American Indian or Alaska Native	1		
Asian	1		
Native Hawaiian or Other Pacific Islander	1		
Black or African American	0		
White	42		
Other	1		
Unknown or Not Reported	7		
Weight Units: kg arithmetic mean standard deviation	-		
Length Units: cm arithmetic mean standard deviation	-		

## End points

### End points reporting groups

Reporting group title	Placebo (combined)
Reporting group description: Placebo (combined)	
Reporting group title	6mg/kg Continuous
Reporting group description: 6mg/kg Continuous	
Reporting group title	6mg/kg Intermittent
Reporting group description: 6mg/kg Intermittent	

### Primary: 6 minute walking distance test (6MWD)

End point title	6 minute walking distance test (6MWD)
End point description:	
End point type	Primary
End point timeframe: Assessments during screening visits, baseline and Weeks 13, 25, 37 and 49.	

End point values	Placebo (combined)	6mg/kg Continuous	6mg/kg Intermittent	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	17	
Units: meter				
arithmetic mean (standard deviation)	403.18 ( $\pm$ 45.131)	427.61 ( $\pm$ 70.045)	394.57 ( $\pm$ 66.952)	

### Statistical analyses

Statistical analysis title	mixed model for repeated measures (MMRM)
Statistical analysis description: The primary efficacy endpoint was the change from baseline at Week 25 in the 6MWD.	
Comparison groups	Placebo (combined) v 6mg/kg Continuous v 6mg/kg Intermittent
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.025
Method	Mixed models analysis





## 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	15.0
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### Reporting groups

Reporting group title	Placebo (combined)
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Reporting group description: -

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

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

<b>Serious adverse events</b>	Placebo (combined)	6mg/kg Intermittent	6mg/kg Continuous
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 18 (11.11%)	2 / 17 (11.76%)	1 / 18 (5.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (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			
Myocarditis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (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
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Glossitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (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
Vomiting			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

<b>Non-serious adverse events</b>	Placebo (combined)	6mg/kg Intermittent	6mg/kg Continuous
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 18 (100.00%)	17 / 17 (100.00%)	17 / 18 (94.44%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Haematoma			
subjects affected / exposed	2 / 18 (11.11%)	1 / 17 (5.88%)	1 / 18 (5.56%)
occurrences (all)	2	1	1

Intra-abdominal haematoma subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1	0 / 18 (0.00%) 0
General disorders and administration site conditions			
Chest pain subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 3	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Fatigue subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 3	3 / 17 (17.65%) 3	0 / 18 (0.00%) 0
Feeling cold subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1	0 / 18 (0.00%) 0
Gait disturbance subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Influenza like illness subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Injection site atrophy subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	3 / 17 (17.65%) 7	1 / 18 (5.56%) 6
Injection site discolouration subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	8 / 17 (47.06%) 28	9 / 18 (50.00%) 32
Injection site erythema subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	8 / 17 (47.06%) 20	8 / 18 (44.44%) 52
Injection site haematoma subjects affected / exposed occurrences (all)	4 / 18 (22.22%) 7	6 / 17 (35.29%) 7	8 / 18 (44.44%) 14
Injection site induration subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	3 / 17 (17.65%) 9	0 / 18 (0.00%) 0
Injection site inflammation			

subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	1 / 18 (5.56%)
occurrences (all)	0	1	2
Injection site macule			
subjects affected / exposed	0 / 18 (0.00%)	2 / 17 (11.76%)	1 / 18 (5.56%)
occurrences (all)	0	8	6
Injection site mass			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
Injection site oedema			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Injection site pain			
subjects affected / exposed	2 / 18 (11.11%)	4 / 17 (23.53%)	2 / 18 (11.11%)
occurrences (all)	2	8	5
Injection site pruritus			
subjects affected / exposed	0 / 18 (0.00%)	3 / 17 (17.65%)	5 / 18 (27.78%)
occurrences (all)	0	8	6
Injection site rash			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	3 / 18 (16.67%)
occurrences (all)	1	0	4
Injection site reaction			
subjects affected / exposed	0 / 18 (0.00%)	3 / 17 (17.65%)	0 / 18 (0.00%)
occurrences (all)	0	4	0
Injection site scab			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Injection site swelling			
subjects affected / exposed	0 / 18 (0.00%)	3 / 17 (17.65%)	2 / 18 (11.11%)
occurrences (all)	0	4	3
Injection site urticaria			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	1 / 18 (5.56%)
occurrences (all)	0	3	2
Irritability			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Malaise			

subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	5 / 18 (27.78%)	5 / 17 (29.41%)	8 / 18 (44.44%)
occurrences (all)	7	5	12
Vessel puncture site haematoma			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Vessel puncture site reaction			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 18 (11.11%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Reproductive system and breast disorders			
Balanitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Penile discharge			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Penile pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Pruritus genital			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 18 (38.89%)	4 / 17 (23.53%)	3 / 18 (16.67%)
occurrences (all)	10	6	5
Epistaxis			

subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	1 / 17 (5.88%) 1	1 / 18 (5.56%) 3
Nasal congestion subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Oropharyngeal pain subjects affected / exposed occurrences (all)	7 / 18 (38.89%) 12	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Rhinorrhoea subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	1 / 17 (5.88%) 1	2 / 18 (11.11%) 3
Psychiatric disorders			
Abnormal behaviour subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Aggression subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Confusional state subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 3	0 / 18 (0.00%) 0
Nightmare subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Investigations			
Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 3	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 2	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Bacterial test positive			

subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Blood fibrinogen abnormal			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Blood fibrinogen decreased			
subjects affected / exposed	2 / 18 (11.11%)	0 / 17 (0.00%)	2 / 18 (11.11%)
occurrences (all)	2	0	5
Blood fibrinogen increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Blood glucose increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Blood pressure systolic increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Body temperature increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Bone density decreased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Coagulation time prolonged			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	3
Complement factor C3 decreased			



subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Cystatin C increased			
subjects affected / exposed	3 / 18 (16.67%)	3 / 17 (17.65%)	3 / 18 (16.67%)
occurrences (all)	3	6	5
Ejection fraction decreased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Electrocardiogram T wave abnormal			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	3
Haptoglobin increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
International normalised ratio increased			
subjects affected / exposed	2 / 18 (11.11%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	3	0	1
Neutrophil toxic granulation present			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Protein total increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Protein urine present			
subjects affected / exposed	2 / 18 (11.11%)	8 / 17 (47.06%)	6 / 18 (33.33%)
occurrences (all)	2	16	12
Prothrombin time prolonged			
subjects affected / exposed	3 / 18 (16.67%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
Red blood cell count increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	4 / 18 (22.22%)
occurrences (all)	1	0	5

Red blood cells urine subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	3 / 17 (17.65%) 5	1 / 18 (5.56%) 1
Red blood cells urine positive subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	4 / 17 (23.53%) 6	5 / 18 (27.78%) 11
Ultrasound liver abnormal subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Urine analysis abnormal subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Urine protein/creatinine ratio increased subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	5 / 17 (29.41%) 13	4 / 18 (22.22%) 15
Weight decreased subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
White blood cell count increased subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	1 / 17 (5.88%) 1	0 / 18 (0.00%) 0
White blood cells urine subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	2 / 17 (11.76%) 6	0 / 18 (0.00%) 0
White blood cells urine positive subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	2 / 17 (11.76%) 3	1 / 18 (5.56%) 1
Injury, poisoning and procedural complications			
Arthropod bite subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Contusion subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	1 / 17 (5.88%) 2	1 / 18 (5.56%) 1
Excoriation			

subjects affected / exposed	4 / 18 (22.22%)	2 / 17 (11.76%)	1 / 18 (5.56%)
occurrences (all)	5	2	2
Face injury			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	7 / 18 (38.89%)	2 / 17 (11.76%)	5 / 18 (27.78%)
occurrences (all)	15	4	5
Head injury			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Joint injury			
subjects affected / exposed	1 / 18 (5.56%)	2 / 17 (11.76%)	1 / 18 (5.56%)
occurrences (all)	1	2	1
Laceration			
subjects affected / exposed	3 / 18 (16.67%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
Ligament sprain			
subjects affected / exposed	3 / 18 (16.67%)	2 / 17 (11.76%)	1 / 18 (5.56%)
occurrences (all)	4	2	1
Limb injury			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Post procedural complication			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Post procedural discomfort			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Post procedural discharge			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Postoperative wound complication			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Procedural pain			

subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 3	4 / 17 (23.53%) 4	3 / 18 (16.67%) 4
Splinter subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Sunburn subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Tooth fracture subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Wound subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Congenital, familial and genetic disorders Phimosis subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Cardiac disorders Bradycardia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Cardiomyopathy subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Sinus tachycardia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Ventricular hypokinesia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1	0 / 18 (0.00%) 0
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Headache			

subjects affected / exposed occurrences (all)	6 / 18 (33.33%) 16	2 / 17 (11.76%) 17	7 / 18 (38.89%) 34
Hypoaesthesia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Nerve compression subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Presyncope subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Tinnitus subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Eye disorders Eye pruritus subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Myopia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1	0 / 18 (0.00%) 0
Ocular hyperaemia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Vision blurred subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 5	4 / 17 (23.53%) 11	7 / 18 (38.89%) 11
Abdominal pain upper			

subjects affected / exposed	0 / 18 (0.00%)	2 / 17 (11.76%)	1 / 18 (5.56%)
occurrences (all)	0	5	1
Aphthous stomatitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Breath odour			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	3 / 18 (16.67%)	0 / 17 (0.00%)	3 / 18 (16.67%)
occurrences (all)	3	0	5
Diarrhoea			
subjects affected / exposed	4 / 18 (22.22%)	2 / 17 (11.76%)	8 / 18 (44.44%)
occurrences (all)	7	5	16
Enteritis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	1 / 18 (5.56%)
occurrences (all)	0	1	3
Faecal incontinence			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Gingival recession			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Glossodynia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	2 / 18 (11.11%)	1 / 17 (5.88%)	2 / 18 (11.11%)
occurrences (all)	4	2	2
Oedema mouth			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Oral mucosal blistering			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
Periodontitis			

subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Swollen tongue			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Tongue discolouration			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Tongue disorder			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	6 / 18 (33.33%)	5 / 17 (29.41%)	7 / 18 (38.89%)
occurrences (all)	10	7	23
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Hepatomegaly			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hair growth abnormal			

subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Heat rash			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Pruritus			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	7 / 18 (38.89%)	1 / 17 (5.88%)	1 / 18 (5.56%)
occurrences (all)	7	1	1
Rash erythematous			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Skin discolouration			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Skin hypopigmentation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Skin lesion			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Albuminuria			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Enuresis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Haematuria			
subjects affected / exposed	0 / 18 (0.00%)	3 / 17 (17.65%)	2 / 18 (11.11%)
occurrences (all)	0	5	5



Myoglobinuria subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Pollakiuria subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Proteinuria subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	3 / 17 (17.65%) 9	2 / 18 (11.11%) 4
Endocrine disorders Goitre subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1	0 / 18 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	2 / 17 (11.76%) 3	0 / 18 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	5 / 18 (27.78%) 7	2 / 17 (11.76%) 3	0 / 18 (0.00%) 0
Flank pain subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Muscle spasms subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Muscular weakness subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Musculoskeletal pain subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Myalgia subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 3	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Pain in extremity			

subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	3 / 17 (17.65%) 3	1 / 18 (5.56%) 1
Spinal disorder subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 2	0 / 18 (0.00%) 0
Infections and infestations			
Bronchitis subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	2 / 17 (11.76%) 2	0 / 18 (0.00%) 0
Ear infection subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Fungal infection subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Gastroenteritis subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	3 / 17 (17.65%) 5	4 / 18 (22.22%) 4
Gastroenteritis viral subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Helicobacter infection subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1	0 / 18 (0.00%) 0
Helminthic infection subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Impetigo subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1	0 / 18 (0.00%) 0
Influenza subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 2	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Lower respiratory tract infection subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1	0 / 18 (0.00%) 0

Nasopharyngitis			
subjects affected / exposed	4 / 18 (22.22%)	3 / 17 (17.65%)	9 / 18 (50.00%)
occurrences (all)	13	7	15
Otitis media			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Pharyngitis			
subjects affected / exposed	1 / 18 (5.56%)	1 / 17 (5.88%)	1 / 18 (5.56%)
occurrences (all)	1	1	1
Postoperative wound infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	6 / 18 (33.33%)	1 / 17 (5.88%)	5 / 18 (27.78%)
occurrences (all)	11	2	11
Sinusitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	2 / 18 (11.11%)
occurrences (all)	1	0	3
Skin candida			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Tinea pedis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Tinea versicolour			
subjects affected / exposed	1 / 18 (5.56%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Tonsillitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	7 / 18 (38.89%)	1 / 17 (5.88%)	5 / 18 (27.78%)
occurrences (all)	13	1	9

Varicella			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
Vitamin D deficiency			
subjects affected / exposed	2 / 18 (11.11%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	2	0	1

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 July 2010	Amendment 1 This amendment corrected the timing of echocardiography assessment at the beginning of the study to be performed during screening (either Screen 1 or Screen 2 visit) and replaced the assessment during the baseline visit. This was to improve safety monitoring of the subject as results of the echocardiograph could be evaluated before the subject was randomised and received first dose of investigational drug.
13 October 2010	Amendment 3. This amendment was implemented to update safety monitoring, technical corrections to prior versions, and corrected the protocol title.
19 July 2011	Amendment 4: This amendment updated the protocol with changes to eligibility to the follow-on extension study, inclusion of additional efficacy endpoints, medical monitor details and change in safety monitoring and stopping criteria. In addition, approval was not granted to recruit healthy volunteers for the accelerometry study within the DMD114117 protocol. Therefore, the healthy volunteer component was removed from the protocol and approval was sought under a separate protocol. Data will be combined with the analysis from this protocol. Minor corrections were made to errors introduced in Amendment 3.
21 June 2012	Amendment 5: This amendment updated renal safety monitoring criteria, reporting updates for SAEs, and added clarification to the Disseminated Intravascular Coagulation criteria. Medical Monitor contact information was also updated as there was a change to the Medical Monitor.

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported