# 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 |

**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) | EMEA-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 |

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 |

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

| Reporting group values | Total | | |
|---|---|---|---|
| Number of subjects | 233 | | |
| Age categorical<br>Units: Subjects | | | |
| 0-85 years and over | 233 | | |
| Age continuous<br>Units: Years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical<br>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] |

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 |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 18.1 |

| Reporting groups | |
|---|---|
| Reporting group title | 6 mg/kg Drisapersen Continuous |
| Reporting group description: - | |
| Reporting group title | Natural History |
| Reporting group description: - | |
| Reporting group title | 6 mg/kg Drisapersen Intermittent |
| 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 | 16 / 228 (7.02%) | 0 / 17 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 33 | 0 | 0 |
| Fibrin D dimer increased | | | |
| subjects affected / exposed | 5 / 228 (2.19%) | 1 / 17 (5.88%) | 0 / 12 (0.00%) |
| occurrences (all) | 6 | 1 | 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 7 / 228 (3.07%) | 0 / 17 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 11 | 0 | 1 |
| Protein urine present | | | |
| subjects affected / exposed | 30 / 228 (13.16%) | 0 / 17 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 115 | 0 | 0 |
| Red blood cells urine | | | |
| subjects affected / exposed | 16 / 228 (7.02%) | 0 / 17 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 37 | 0 | 0 |
| Red blood cells urine positive | | | |
| subjects affected / exposed | 25 / 228 (10.96%) | 0 / 17 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 53 | 0 | 0 |
| Urine analysis abnormal | | | |
| subjects affected / exposed | 1 / 228 (0.44%) | 0 / 17 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 3 | 0 | 2 |
| Urine protein/creatinine ratio increased | | | |
| subjects affected / exposed | 20 / 228 (8.77%) | 0 / 17 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 40 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 22 / 228 (9.65%) | 1 / 17 (5.88%) | 0 / 12 (0.00%) |
| occurrences (all) | 35 | 1 | 0 |
| Fall | | | |
| subjects affected / exposed | 51 / 228 (22.37%) | 0 / 17 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 134 | 0 | 0 |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 228 (0.44%) | 0 / 17 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 0 | 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