Clinical trial results:
An open-label extension study of the long-term safety, tolerability and efficacy of drisapersen in subjects with Duchenne Muscular Dystrophy.

Summary

EudraCT number	2015-001955-54
Trial protocol	NL DE BE ES
Global end of trial date	07 September 2016

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	BMN-051-302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02636686
WHO universal trial number (UTN)	-
Other trial identifiers	Duchenne Muscular Dystrophy: DMD

Notes:

Sponsors

Sponsor organisation name	BioMarin Pharmaceutical Inc.
Sponsor organisation address	105 Digital Drive, Novato, United States, CA 94949
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)	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	Interim
Date of interim/final analysis	17 October 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 September 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of subcutaneous or intravenous drisapersen in subjects with DMD correctable by drisapersen-induced DMD exon 51 skipping who have previously participated in an eligible study.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 September 2015
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	Belgium: 4
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	19
EEA total number of subjects	17

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)	5
Adolescents (12-17 years)	11

Adults (18-64 years)	3
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All subjects entering the treatment phase are required to provide written informed consent/assent (along with parental/guardian consent if applicable) and have confirmation that the inclusion and exclusion criteria have been evaluated by a medically qualified designee, including medical history and concurrent medication review.

Period 1

Period 1 title	BMN051-302 (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	6 mg/kg/wk SC

Arm description:

6 mg/kg/wk SC

Arm type	Experimental
Investigational medicinal product name	drisapersen
Investigational medicinal product code	BMN051
Other name	GSK2402968, PRO051
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV dosing of 3mg/kg/week over a 1 hour infusion time

Arm title	3 mg/kg/wk IV

Arm description:

3 mg/kg/wk IV

Arm type	Experimental
Investigational medicinal product name	drisapersen
Investigational medicinal product code	BMN051
Other name	GSK2402968, PRO051
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV dosing of 3mg/kg/week over a 1 hour infusion time

Number of subjects in period 1	6 mg/kg/wk SC	3 mg/kg/wk IV
Started	11	8
Completed	0	0
Not completed	11	8
Consent withdrawn by subject	1	-
Death	1	-
Study Terminated by Sponsor	9	7
Missing	-	1

Baseline characteristics

Reporting groups	
Reporting group title	6 mg/kg/wk SC
Reporting group description: 6 mg/kg/wk SC	
Reporting group title	3 mg/kg/wk IV
Reporting group description: 3 mg/kg/wk IV	

Reporting group values	6 mg/kg/wk SC	3 mg/kg/wk IV	Total
Number of subjects	11	8	19
Age categorical Units: Subjects			
9 - 11	4	1	5
12 - 17	4	7	11
>= 18	3	0	3
Age continuous Units: Years			
arithmetic mean	13.8	13.3	
standard deviation	± 4.31	± 1.98	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	11	8	19
Ethnicity Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	10	7	17
Unknown or Not Reported	1	0	1

End points

End points reporting groups

Reporting group title	6 mg/kg/wk SC
Reporting group description: 6 mg/kg/wk SC	
Reporting group title	3 mg/kg/wk IV
Reporting group description: 3 mg/kg/wk IV	

Primary: Safety

End point title	Safety[1]
End point description: To evaluate the long-term safety and tolerability of subcutaneous or intravenous drisapersen in subjects with DMD correctable by drisapersen-induced DMD exon 51 skipping who have previously participated in an eligible study.	
End point type	Primary
End point timeframe: Long term	

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 is terminated early and only safety data is presented.

End point values	6 mg/kg/wk SC	3 mg/kg/wk IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	8		
Units: Safety	0	0		

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	3 mg/kg/wk IV
Reporting group description: -	
Reporting group title	6 mg/kg/wk SC
Reporting group description: -	

Serious adverse events	3 mg/kg/wk IV	6 mg/kg/wk SC	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events			
Congenital, familial and genetic disorders			
Duchenne muscular dystrophy			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	3 mg/kg/wk IV	6 mg/kg/wk SC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 8 (75.00%)	11 / 11 (100.00%)	
Investigations			
Complement factor C3 decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Urine protein/creatinine ratio increased			

subjects affected / exposed	1 / 8 (12.50%)	1 / 11 (9.09%)	
occurrences (all)	4	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 8 (0.00%)	2 / 11 (18.18%)	
occurrences (all)	0	4	
Lower limb fracture			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Tibia fracture			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Cyanosis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 8 (12.50%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 8 (12.50%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Application site hypersensitivity			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Chills			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Influenza like illness			
subjects affected / exposed	1 / 8 (12.50%)	2 / 11 (18.18%)	
occurrences (all)	2	2	

Injection site discolouration			
subjects affected / exposed	0 / 8 (0.00%)	2 / 11 (18.18%)	
occurrences (all)	0	3	
Injection site dryness			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	4	
Injection site erythema			
subjects affected / exposed	0 / 8 (0.00%)	7 / 11 (63.64%)	
occurrences (all)	0	35	
Injection site haematoma			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	2	
Injection site haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Injection site hypoaesthesia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Injection site induration			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	5	
Injection site vesicles			
subjects affected / exposed	0 / 8 (0.00%)	2 / 11 (18.18%)	
occurrences (all)	0	5	
Non-cardiac chest pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Eye disorders			
Eye irritation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	2 / 8 (25.00%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 8 (12.50%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Hypoventilation			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Rash erythematous			
subjects affected / exposed	1 / 8 (12.50%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Skin hyperpigmentation			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	3 / 8 (37.50%)	1 / 11 (9.09%)	
occurrences (all)	6	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Back pain			

subjects affected / exposed	1 / 8 (12.50%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Joint swelling			
subjects affected / exposed	1 / 8 (12.50%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Muscle contracture			
subjects affected / exposed	1 / 8 (12.50%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Myalgia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	1 / 8 (12.50%)	1 / 11 (9.09%)	
occurrences (all)	2	1	
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 8 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	2 / 11 (18.18%)	
occurrences (all)	0	2	
Rhinitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	2 / 8 (25.00%)	0 / 11 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 July 2015	Protocol Amendment 1

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported