



## 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
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##### 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
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<b>Arm title</b>	6 mg/kg/wk SC
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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

<b>Arm title</b>	3 mg/kg/wk IV
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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

<b>Number of subjects in period 1</b>	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
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Reporting group description:

6 mg/kg/wk SC

Reporting group title	3 mg/kg/wk IV
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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 <sup>[1]</sup>
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
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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	3 mg/kg/wk IV
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Reporting group description: -

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

<b>Serious adverse events</b>	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 %

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

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

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

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

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported