Clinical trial results:
A phase IIb, open-label study to assess the efficacy, safety, pharmacodynamics and pharmacokinetics of multiple subcutaneous doses of PRO045 in subjects with Duchenne muscular dystrophy

Summary

EudraCT number	2011-005040-10
Trial protocol	BE GB IT FR
Global end of trial date	31 August 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	PRO045-CLIN-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01826474
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BioMarin Pharmaceutical Inc.
Sponsor organisation address	105 Digital Drive, Novato, United States, CA 94949
Public contact	Clinical Trials, BioMarin Pharmaceutical Inc., clinicaltrials@bmrn.com
Scientific contact	Clinical Trials, 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-000136-PIP01-12
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	21 October 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 August 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of PRO045 after 48 weeks treatment in ambulant subjects with Duchenne muscular dystrophy.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 December 2012
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: 3
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	United Kingdom: 3
Worldwide total number of subjects	15
EEA total number of subjects	15

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)	13
Adolescents (12-17 years)	2
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:

Visit S1 will include confirmation of consent and evaluation of the full DNA diagnostic report and the inclusion and exclusion criteria. Visit S2 should not be conducted until enrolment into any given dose group is agreed. S2 will be conducted within 2 weeks prior to first dose. S2 will include evaluation of the inclusion and exclusion criteria.

Period 1

Period 1 title	BMN045 (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	BMN045 0.15 mg/kg

Arm description:

BMN045 0.15 mg/kg

Arm type	Experimental
Investigational medicinal product name	BMN045
Investigational medicinal product code	BMN045
Other name	PRO045
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects will each receive a single dose of 0.15 mg/kg BMN 045 by subcutaneous injection once per week.

Arm title	BMN045 1.0 mg/kg

Arm description:

BMN045 1.0 mg/kg

Arm type	Experimental
Investigational medicinal product name	BMN045
Investigational medicinal product code	BMN045
Other name	PRO045
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use, Intravenous use

Dosage and administration details:

Subjects will each receive one single dose of intravenous BMN 045 at the corresponding dose level (1mg/kg) to assess pharmacokinetic and bioavailability compared to the subcutaneous route. One week later, and for every subsequent week until dose up-titration, the same dose will be administered by subcutaneous injection.
The first BMN 045 administration will be by IV infusion over three hours.

Arm title	BMN045 3.0 mg/kg

Arm description:

BMN045 3.0 mg/kg

Arm type	Experimental

Investigational medicinal product name	BMN045
Investigational medicinal product code	BMN045
Other name	PRO045
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Subjects will each receive one single dose of intravenous BMN 045 at the corresponding dose level (3mg/kg) to assess pharmacokinetic and bioavailability compared to the subcutaneous route. One week later, and for every subsequent week until dose up-titration, the same dose will be administered by subcutaneous injection.
The first BMN 045 administration will be by IV infusion over three hours.

Arm title	BMN045 6.0 mg/kg

Arm description:

BMN045 6.0 mg/kg

Arm type	Experimental
Investigational medicinal product name	BMN045
Investigational medicinal product code	BMN045
Other name	PRO045
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Subjects will each receive one single dose of intravenous BMN 045 at the corresponding dose level (6mg/kg) to assess pharmacokinetic and bioavailability compared to the subcutaneous route. One week later, and for every subsequent week until dose up-titration, the same dose will be administered by subcutaneous injection.
The first BMN 045 administration will be by IV infusion over three hours.

Arm title	BMN045 9.0 mg/kg

Arm description:

BMN045 9.0 mg/kg

Arm type	Experimental
Investigational medicinal product name	BMN045
Investigational medicinal product code	BMN045
Other name	PRO045
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Subjects will each receive one single dose of intravenous BMN 045 at the corresponding dose level (9mg/kg) to assess pharmacokinetic and bioavailability compared to the subcutaneous route. One week later, and for every subsequent week until dose up-titration, the same dose will be administered by subcutaneous injection.
The first BMN 045 administration will be by IV infusion over three hours.

Number of subjects in period 1	BMN045 0.15 mg/kg	BMN045 1.0 mg/kg	BMN045 3.0 mg/kg
Started	3	6	9
Completed	0	0	0
Not completed	3	6	9
Other	-	-	1
Study Subject Withdrawal by Parent or Guardian	3	4	4
Study Terminated by Sponsor	-	2	4

Number of subjects in period 1	BMN045 6.0 mg/kg	BMN045 9.0 mg/kg
Started	12	15
Completed	0	0
Not completed	12	15
Other	1	1
Study Subject Withdrawal by Parent or Guardian	4	5
Study Terminated by Sponsor	7	9

Baseline characteristics

Reporting groups	
Reporting group title	BMN045 0.15 mg/kg
Reporting group description: BMN045 0.15 mg/kg	
Reporting group title	BMN045 1.0 mg/kg
Reporting group description: BMN045 1.0 mg/kg	
Reporting group title	BMN045 3.0 mg/kg
Reporting group description: BMN045 3.0 mg/kg	
Reporting group title	BMN045 6.0 mg/kg
Reporting group description: BMN045 6.0 mg/kg	
Reporting group title	BMN045 9.0 mg/kg
Reporting group description: BMN045 9.0 mg/kg	

Reporting group values	BMN045 0.15 mg/kg	BMN045 1.0 mg/kg	BMN045 3.0 mg/kg
Number of subjects	3	6	9
Age categorical Units: Subjects			
6 - 12	3	6	9
Age continuous Units: Years			
arithmetic mean	10	6.7	8.3
standard deviation	± 3.46	± 1.15	± 0.58
Gender categorical Units: Subjects			
Female	0	0	0
Male	3	6	9
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	0	0	2
Unknown or Not Reported	3	6	7
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	0	0
Other	3	6	9
Not Collected	0	0	0

Weight			
Units: kg			
arithmetic mean	36.5	25.83	27.9
standard deviation	± 13.115	± 8.119	± 6.092
Length			
Units: cm			
arithmetic mean	1.226	1.183	1.277
standard deviation	± 0.132	± 0.059	± 0.077

Reporting group values	BMN045 6.0 mg/kg	BMN045 9.0 mg/kg	Total
Number of subjects	12	15	15
Age categorical			
Units: Subjects			
6 - 12	12	15	15
Age continuous			
Units: Years			
arithmetic mean	8.3	9	
standard deviation	± 1.53	± 1.73	-
Gender categorical			
Units: Subjects			
Female	0	0	0
Male	12	15	15
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	5	8	8
Unknown or Not Reported	7	7	7
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	0	0
Other	12	15	15
Not Collected	0	0	0
Weight			
Units: kg			
arithmetic mean	28.57	31.67	
standard deviation	± 5.437	± 9.074	-
Length			
Units: cm			
arithmetic mean	1.273	1.263	
standard deviation	± 0.058	± 0.079	-

End points

End points reporting groups

Reporting group title	BMN045 0.15 mg/kg
Reporting group description: BMN045 0.15 mg/kg	
Reporting group title	BMN045 1.0 mg/kg
Reporting group description: BMN045 1.0 mg/kg	
Reporting group title	BMN045 3.0 mg/kg
Reporting group description: BMN045 3.0 mg/kg	
Reporting group title	BMN045 6.0 mg/kg
Reporting group description: BMN045 6.0 mg/kg	
Reporting group title	BMN045 9.0 mg/kg
Reporting group description: BMN045 9.0 mg/kg	

Primary: 6 MWD

End point title	6 MWD[1]
End point description: To assess the efficacy of BMN 045 after 48 weeks of treatment in ambulant subjects with DMD.	
End point type	Primary
End point timeframe: 48 weeks	

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: Due to the early termination of this study, no efficacy outcomes are reported.

End point values	BMN045 0.15 mg/kg	BMN045 1.0 mg/kg	BMN045 3.0 mg/kg	BMN045 6.0 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[2]	0[3]	0[4]	0[5]
Units: meter				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[2] - Due to the early termination of this study, no efficacy outcomes are reported.

[3] - Due to the early termination of this study, no efficacy outcomes are reported.

[4] - Due to the early termination of this study, no efficacy outcomes are reported.

[5] - Due to the early termination of this study, no efficacy outcomes are reported.

End point values	BMN045 9.0 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: meter				
arithmetic mean (standard deviation)	()			

Notes:
[6] - Due to the early termination of this study, no efficacy outcomes are reported.

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	19

Reporting groups	
Reporting group title	BMN045 0.15 mg/kg
Reporting group description: -	
Reporting group title	BMN045 1.0 mg/kg
Reporting group description: -	
Reporting group title	BMN045 3.0 mg/kg
Reporting group description: -	
Reporting group title	BMN045 6.0 mg/kg
Reporting group description: -	
Reporting group title	BMN045 9.0 mg/kg
Reporting group description: -	

Serious adverse events	BMN045 0.15 mg/kg	BMN045 1.0 mg/kg	BMN045 3.0 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	BMN045 6.0 mg/kg	BMN045 9.0 mg/kg	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Infections and infestations			
Respiratory tract infection			

subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	BMN045 0.15 mg/kg	BMN045 1.0 mg/kg	BMN045 3.0 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	6 / 6 (100.00%)	7 / 9 (77.78%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	1
Injection site laceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Injection site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Injection site vesicles			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Malaise			

subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Nasal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Oropharyngeal pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Aggression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Delusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Insomnia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Activated partial thromboplastin time shortened			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Alpha 1 microglobulin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood fibrinogen decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood immunoglobulin g decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Complement factor c3 decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Complement factor decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cystatin c increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Glomerular filtration rate increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Glutamate dehydrogenase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Monocyte chemotactic protein-1 increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Platelet count increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Protein urine			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	3 / 9 (33.33%)
occurrences (all)	0	4	10
Protein urine present			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Serum ferritin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Urinary casts			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Urine protein/creatinine ratio increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
White blood cells urine positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Foot fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Head injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Post procedural complication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Post procedural contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Procedural complication			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Procedural pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 3 (66.67%)	2 / 6 (33.33%)	1 / 9 (11.11%)
occurrences (all)	7	3	2
Lethargy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Platelet disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Conjunctival hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Eye irritation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Anal fissure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Breath odour			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Food poisoning			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Noninfective gingivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Tooth disorder			

subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Tooth impacted			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Angioedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Drug eruption			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Ingrowing nail			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Petechiae			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0

Rash			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Rash erythematous			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Spider naevus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Haemarthrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Joint instability			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Myalgia			

subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Fungal skin infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 9 (11.11%)
occurrences (all)	0	1	2
Helminthic infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal infection			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	1 / 9 (11.11%)
occurrences (all)	0	2	2
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	2 / 3 (66.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	4	0	0
Tonsillitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 3 (66.67%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	4	0	2
Viral infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	BMN045 6.0 mg/kg	BMN045 9.0 mg/kg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	15 / 15 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
General disorders and administration			

site conditions			
Fatigue			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			
subjects affected / exposed	1 / 12 (8.33%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Injection site laceration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Injection site pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Injection site vesicles			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	0 / 12 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	4	
Pyrexia			
subjects affected / exposed	3 / 12 (25.00%)	2 / 15 (13.33%)	
occurrences (all)	4	5	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	2 / 12 (16.67%)	0 / 15 (0.00%)	
occurrences (all)	3	0	
Cough			
subjects affected / exposed	3 / 12 (25.00%)	3 / 15 (20.00%)	
occurrences (all)	3	3	
Nasal obstruction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Rhinitis allergic			

subjects affected / exposed	1 / 12 (8.33%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Rhinorrhoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Aggression			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Delusion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 12 (8.33%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Activated partial thromboplastin time shortened			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Alanine aminotransferase increased			
subjects affected / exposed	2 / 12 (16.67%)	3 / 15 (20.00%)	
occurrences (all)	2	3	
Alpha 1 microglobulin increased			
subjects affected / exposed	2 / 12 (16.67%)	3 / 15 (20.00%)	
occurrences (all)	2	6	
Blood fibrinogen decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Blood immunoglobulin g decreased			

subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
C-reactive protein increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Complement factor c3 decreased			
subjects affected / exposed	6 / 12 (50.00%)	11 / 15 (73.33%)	
occurrences (all)	15	22	
Complement factor decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Cystatin c increased			
subjects affected / exposed	0 / 12 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 12 (25.00%)	1 / 15 (6.67%)	
occurrences (all)	3	1	
Glomerular filtration rate increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Glutamate dehydrogenase increased			
subjects affected / exposed	3 / 12 (25.00%)	0 / 15 (0.00%)	
occurrences (all)	3	0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 12 (8.33%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Monocyte chemotactic protein-1 increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	4	
Platelet count decreased			
subjects affected / exposed	9 / 12 (75.00%)	9 / 15 (60.00%)	
occurrences (all)	30	22	
Platelet count increased			

subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Protein urine			
subjects affected / exposed	10 / 12 (83.33%)	12 / 15 (80.00%)	
occurrences (all)	87	43	
Protein urine present			
subjects affected / exposed	3 / 12 (25.00%)	3 / 15 (20.00%)	
occurrences (all)	9	8	
Serum ferritin increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Urinary casts			
subjects affected / exposed	0 / 12 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	3	
Urine protein/creatinine ratio increased			
subjects affected / exposed	6 / 12 (50.00%)	7 / 15 (46.67%)	
occurrences (all)	13	14	
White blood cells urine positive			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 12 (16.67%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Fall			
subjects affected / exposed	2 / 12 (16.67%)	1 / 15 (6.67%)	
occurrences (all)	2	5	
Foot fracture			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Head injury			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Joint injury			

subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Ligament sprain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Post procedural complication			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Post procedural contusion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Procedural complication			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Procedural pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	3	
Headache			
subjects affected / exposed	3 / 12 (25.00%)	2 / 15 (13.33%)	
occurrences (all)	11	11	
Lethargy			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Syncope			
subjects affected / exposed	1 / 12 (8.33%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Blood and lymphatic system disorders			

Lymphadenopathy			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Platelet disorder			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 12 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	3	
Eye disorders			
Conjunctival hyperaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Eye irritation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 12 (33.33%)	0 / 15 (0.00%)	
occurrences (all)	6	0	
Abdominal pain upper			
subjects affected / exposed	3 / 12 (25.00%)	4 / 15 (26.67%)	
occurrences (all)	5	6	
Anal fissure			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Breath odour			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	2 / 12 (16.67%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Diarrhoea			
subjects affected / exposed	1 / 12 (8.33%)	2 / 15 (13.33%)	
occurrences (all)	10	3	
Food poisoning			

subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Gastritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	0 / 12 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Noninfective gingivitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Stomatitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Tooth disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Tooth impacted			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	1 / 12 (8.33%)	1 / 15 (6.67%)	
occurrences (all)	1	4	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Angioedema			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Decubitus ulcer			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Ecchymosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	

Drug eruption			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	1 / 12 (8.33%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Ingrowing nail			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Petechiae			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	1 / 12 (8.33%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Rash erythematous			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Spider naevus			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Urticaria			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 12 (16.67%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Back pain			

subjects affected / exposed	1 / 12 (8.33%)	1 / 15 (6.67%)	
occurrences (all)	1	2	
Haemarthrosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Joint instability			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Musculoskeletal pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Neck pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	2 / 12 (16.67%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Ear infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Fungal skin infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	

Gastroenteritis			
subjects affected / exposed	2 / 12 (16.67%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Helminthic infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gastrointestinal infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	1 / 12 (8.33%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Localised infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	4 / 12 (33.33%)	6 / 15 (40.00%)	
occurrences (all)	4	8	
Oropharyngeal candidiasis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Rhinitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Tonsillitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	2 / 12 (16.67%)	1 / 15 (6.67%)	
occurrences (all)	3	4	
Viral infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 15 (0.00%)	
occurrences (all)	1	0	

Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 15 (6.67%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2012	Prot Amt 1
16 August 2013	Prot Amt 2
07 January 2016	Prot Amt 3

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported