Clinical trial results:
Extension of the CBYM338B2203 Phase IIb/III study to evaluate the long-term efficacy, safety and tolerability of intravenous BYM338 in patients with sporadic inclusion body myositis

Summary

EudraCT number	2015-001411-12
Trial protocol	FR NL DK GB BE IT
Global end of trial date	13 February 2017

Results information

Result version number	v1 (current)
This version publication date	28 February 2018
First version publication date	28 February 2018

Trial information

Trial identification

Sponsor protocol code	CBYM338B2203E1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02573467
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of intravenously administered bimagrumab in the treatment of sIBM as assessed by vital signs, electrocardiogram (ECG), clinical laboratory variables, and adverse events (AEs) monitoring. In addition, to further evaluate the effect of three bimagrumab dose regimens against placebo in increasing the distance traveled as measured by the 6-minute walking distance test (6MWD).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 November 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	Australia: 37
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Denmark: 12
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	United Kingdom: 21
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Japan: 15
Country: Number of subjects enrolled	Netherlands: 18
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	United States: 77
Worldwide total number of subjects	211
EEA total number of subjects	81

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	53
From 65 to 84 years	156
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Participants entered extension study treatment period after completing the core study and continued on the study drug to which they were randomized in the core study (one of 3 bimagrumab doses (1mg/kg, 3mg/kg or 10mg/kg) or placebo). Participants discontinued from the treatment period were to enter a 6-month, treatment-free Follow-up Period (FUP).

Pre-assignment

Screening details:

All participants (N=211) were discontinued from the double-blind treatment period, 178 of whom entered the FUP. Overall 154 participants completed the FUP and 20 discontinued due to subject/guardian decision and 1 for technical reasons. Three discontinued FUP due to death (one each in the 10mg/kg, 3mg/kg, and placebo groups).

Period 1

Period 1 title	Double-blind treatment epoch (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	BYM338/bimagrumab 10 mg/kg

Arm description:

Participants received BYM338 10 mg/kg administered via intravenous infusion every 4 weeks for up to a maximum of 8 months after which they entered a 6-month, treatment-free follow-up period.

Arm type	Experimental
Investigational medicinal product name	Bimagrumab
Investigational medicinal product code	BYM338
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received BYM338 10 mg/kg administered via intravenous infusion every 4 weeks.

Arm title	BYM338/bimagrumab 3 mg/kg

Arm description:

Participants received BYM338 3 mg/kg administered via intravenous infusion every 4 weeks for up to a maximum of 8 months after which they entered a 6-month, treatment-free follow-up period.

Arm type	Experimental
Investigational medicinal product name	Bimagrumab
Investigational medicinal product code	BYM338
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received BYM338 3 mg/kg administered via intravenous infusion every 4 weeks.

Arm title	BYM338/bimagrumab 1 mg/kg

Arm description:

Participants received BYM338 1 mg/kg administered via intravenous infusion every 4 weeks for up to a maximum of 8 months after which they entered a 6-month, treatment-free follow-up period.

Arm type	Experimental

Investigational medicinal product name	Bimagrumab
Investigational medicinal product code	BYM338
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received BYM338 1 mg/kg administered via intravenous infusion every 4 weeks.

Arm title	Placebo

Arm description:

Participants received placebo administered via intravenous infusion every 4 weeks for up to a maximum of 8 months after which they entered a 6-month, treatment-free follow-up period.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received placebo administered via intravenous infusion every 4 weeks.

Number of subjects in period 1	BYM338/bimagrumab 10 mg/kg	BYM338/bimagrumab 3 mg/kg	BYM338/bimagrumab 1 mg/kg
Started	53	52	51
Full analysis set	53	52	51
Completed	0	0	0
Not completed	53	52	51
Study Terminated by sponsor	50	51	48
Adverse event, non-fatal	1	-	1
Withdrawal by subject	2	1	1
Lack of efficacy	-	-	1

Number of subjects in period 1	Placebo
Started	55
Full analysis set	55
Completed	0
Not completed	55
Study Terminated by sponsor	55
Adverse event, non-fatal	-
Withdrawal by subject	-
Lack of efficacy	-

Baseline characteristics

Reporting groups	
Reporting group title	BYM338/bimagrumab 10 mg/kg
Reporting group description:	
Participants received BYM338 10 mg/kg administered via intravenous infusion every 4 weeks for up to a maximum of 8 months after which they entered a 6-month, treatment-free follow-up period.	
Reporting group title	BYM338/bimagrumab 3 mg/kg
Reporting group description:	
Participants received BYM338 3 mg/kg administered via intravenous infusion every 4 weeks for up to a maximum of 8 months after which they entered a 6-month, treatment-free follow-up period.	
Reporting group title	BYM338/bimagrumab 1 mg/kg
Reporting group description:	
Participants received BYM338 1 mg/kg administered via intravenous infusion every 4 weeks for up to a maximum of 8 months after which they entered a 6-month, treatment-free follow-up period.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo administered via intravenous infusion every 4 weeks for up to a maximum of 8 months after which they entered a 6-month, treatment-free follow-up period.	

Reporting group values	BYM338/bimagrumab 10 mg/kg	BYM338/bimagrumab 3 mg/kg	BYM338/bimagrumab 1 mg/kg
Number of subjects	53	52	51
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	11	19	11
From 65-84 years	42	32	39
85 years and over	0	1	1
Age Continuous Units: Years			
arithmetic mean	69.2	67.3	70.0
standard deviation	± 8.19	± 9.04	± 7.69
Gender, Male/Female Units: Subjects			
Female	18	19	17
Male	35	33	34

Reporting group values	Placebo	Total	
Number of subjects	55	211	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	

Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	12	53	
From 65-84 years	43	156	
85 years and over	0	2	
Age Continuous			
Units: Years			
arithmetic mean	69.9		
standard deviation	± 7.95	-	
Gender, Male/Female			
Units: Subjects			
Female	19	73	
Male	36	138	

End points

End points reporting groups

Reporting group title	BYM338/bimagrumab 10 mg/kg
Reporting group description:	
Participants received BYM338 10 mg/kg administered via intravenous infusion every 4 weeks for up to a maximum of 8 months after which they entered a 6-month, treatment-free follow-up period.	
Reporting group title	BYM338/bimagrumab 3 mg/kg
Reporting group description:	
Participants received BYM338 3 mg/kg administered via intravenous infusion every 4 weeks for up to a maximum of 8 months after which they entered a 6-month, treatment-free follow-up period.	
Reporting group title	BYM338/bimagrumab 1 mg/kg
Reporting group description:	
Participants received BYM338 1 mg/kg administered via intravenous infusion every 4 weeks for up to a maximum of 8 months after which they entered a 6-month, treatment-free follow-up period.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo administered via intravenous infusion every 4 weeks for up to a maximum of 8 months after which they entered a 6-month, treatment-free follow-up period.	

Primary: Number of participants with adverse events (AEs), serious adverse events (SAEs) and deaths.

End point title	Number of participants with adverse events (AEs), serious adverse events (SAEs) and deaths.[1]
End point description:	
Safety monitoring was conducted throughout the study. AEs starting on or after the day of first administration of extension study drug until last administration of study drug + 56 days are considered. SAEs starting on or after the day of first administration of extension study drug are considered. Deaths which occurred on or after the day of first administration of extension study drug are considered.	
End point type	Primary
End point timeframe:	
to end of study (up to 14 months, including the 6-month treatment-free follow-up period)	

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: Statistical analysis does not apply to this end point.

End point values	BYM338/bimagrumab 10 mg/kg	BYM338/bimagrumab 3 mg/kg	BYM338/bimagrumab 1 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	52	51	55
Units: Participants				
Adverse events|	48	50	44	49
Serious adverse events|	12	10	7	8
Deaths|	1	1	1	2

Statistical analyses

No statistical analyses for this end point

Primary: Change from core study baseline in 6 Minute Walking Distance Test (6MWD)

End point title	Change from core study baseline in 6 Minute Walking Distance Test (6MWD)[2]

End point description:

The 6MWD test measures the distance (in meters) that a participant can walk in a 6 minute time frame. A positive change from baseline indicates improvement. The efficacy analysis and time points were based on windowed visits relative to the first dose of the double-blind treatment in the core study.

End point type	Primary

End point timeframe:

Core study baseline, weeks 52, 78, 104

Notes:

[2] - 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: Descriptive statistics only were calculated for this end point.

End point values	BYM338/bimagrumab 10 mg/kg	BYM338/bimagrumab 3 mg/kg	BYM338/bimagrumab 1 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	52	51	55
Units: meters				
arithmetic mean (standard deviation)				
Week 52 (n=53,52,51,54)|	6.88 (± 68.948)	9.48 (± 81.676)	-14.26 (± 81.029)	-5.98 (± 78.817)
Week 78 (n=52,52,50,54)|	-5.25 (± 122.002)	-9.73 (± 68.302)	-18.66 (± 81.536)	-32.78 (± 96.494)
Week 104 (n=32,34,37,39)|	-22.68 (± 102.549)	-50.58 (± 118.012)	-25.08 (± 95.737)	-61.30 (± 107.399)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from core study baseline in quadriceps Quantitative Muscle Testing (QMT) on the right side

End point title	Change from core study baseline in quadriceps Quantitative Muscle Testing (QMT) on the right side

End point description:

Quantitative Muscle Testing (QMT) was used to describe the long-term evolution of quadriceps muscle strength on the right side. The QMT was performed using the same portable fixed dynamometry (PFD) used in the core study. A negative change from baseline indicates deterioration. The efficacy analysis and time points were based on windowed visits relative to the first dose of the double-blind treatment in the core study.

End point type	Secondary

End point timeframe:

Core study baseline, week 52, week 78, week 104

End point values	BYM338/bimagrumab 10 mg/kg	BYM338/bimagrumab 3 mg/kg	BYM338/bimagrumab 1 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	52	51	55
Units: newtons				
arithmetic mean (standard deviation)				
Week 52 (n=48,49,51,55)|	-6.29 (± 31.121)	-19.70 (± 77.820)	-5.62 (± 32.245)	-14.22 (± 27.577)
Week 78 (n=46,49,49,53)|	-9.43 (± 41.285)	-23.76 (± 73.729)	-17.04 (± 25.696)	-21.02 (± 31.391)
Week 104 (n=33,33,37,37)|	-11.92 (± 35.243)	-16.99 (± 34.379)	-18.63 (± 37.968)	-21.91 (± 39.985)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from core study baseline in sporadic inclusion body myositis (sIBM) functional assessment (sIFA) score

End point title	Change from core study baseline in sporadic inclusion body myositis (sIBM) functional assessment (sIFA) score

End point description:

Self-reported physical function was assessed by a newly developed patient reported outcome named sporadic inclusion body myositis (sIBM) functional assessment (sIFA). The sIFA consists of 11 items scored on an 11 point numerical rating scale from 0 (no difficulty) to 10 (unable to do) across 3 domains: upper body functioning, lower body functioning and general functioning. Participants completed the assessment where the recall period was the past week prior to completing the patient reported outcome (PRO). The total score on the sIFA scale ranges from 0 (minimum) to 110 (maximum). Higher values represent a worse outcome. A positive change from baseline indicates deterioration. The efficacy analysis and time points were based on windowed visits relative to the first dose of the double-blind treatment in the core study.

End point type	Secondary

End point timeframe:

Core study baseline, week 52, week 78, week 104

End point values	BYM338/bimagrumab 10 mg/kg	BYM338/bimagrumab 3 mg/kg	BYM338/bimagrumab 1 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	52	51	55
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 52 (n=53,52,49,52)|	-1.34 (± 15.249)	1.80 (± 11.910)	3.17 (± 11.380)	5.16 (± 13.889)
Week 78 (n=53,51,48,54)|	-0.27 (± 13.745)	5.33 (± 13.099)	6.52 (± 12.918)	7.41 (± 14.410)
Week 104 (n=38,37,35,40)|	3.54 (± 14.998)	8.04 (± 16.861)	5.97 (± 12.849)	7.39 (± 15.580)

Statistical analyses

No statistical analyses for this end point

Secondary: Estimated annual number of falls per participant within treatment group

End point title	Estimated annual number of falls per participant within treatment group

End point description:

Participants documented any fall occurrences in a paper diary during the study.

End point type	Secondary

End point timeframe:

Core baseline to end of extension double-blind treatment (up to a maximum of 32 months)

End point values	BYM338/bimagrumab 10 mg/kg	BYM338/bimagrumab 3 mg/kg	BYM338/bimagrumab 1 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	52	51	55
Units: Annual number of falls per participant				
number (not applicable)	4.164	3.879	3.480	3.835

Statistical analyses

No statistical analyses for this end point

Secondary: Change from core study baseline in Short Physical Performance Battery (SPPB) score

End point title	Change from core study baseline in Short Physical Performance Battery (SPPB) score

End point description:

The SPPB evaluated lower extremities function by testing gait speed, ability to keep standing balance and time to rise from a chair five times. The sub-score for each test ranged from 0 to 4. The summary score, which was a summation of scores from the 3 tests, ranged from 0 to 12. An increase in score indicates improvement in physical performance. A negative change from baseline indicates deterioration. The efficacy analysis and time points were based on windowed visits relative to the first dose of the double-blind treatment in the core study.

End point type	Secondary

End point timeframe:

Core study baseline, week 52, week 78, week 104

End point values	BYM338/bimagrumab 10 mg/kg	BYM338/bimagrumab 3 mg/kg	BYM338/bimagrumab 1 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	52	51	55
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 52 (n=53,52,51,55)|	0.3 (± 1.73)	0.2 (± 1.61)	-0.4 (± 1.74)	-0.3 (± 1.31)
Week 78 (n=53,52,50,55)|	-0.5 (± 2.58)	-0.1 (± 1.54)	-0.4 (± 1.69)	-0.9 (± 1.92)
Week 104 (n=38,38,39,41)|	-1.4 (± 3.29)	-0.9 (± 2.77)	-1.1 (± 2.56)	-1.3 (± 2.35)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in muscles of the thigh

End point title	Change in muscles of the thigh

End point description:

Magnetic resonance imaging (MRI) was planned to be used to characterize changes in muscles of the thigh in a subset of patients.

End point type	Secondary

End point timeframe:

up to 1 year, up to 2 years

End point values	BYM338/bimagrumab 10 mg/kg	BYM338/bimagrumab 3 mg/kg	BYM338/bimagrumab 1 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[3]	0[4]	0[5]	0[6]
Units: Percentage				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[3] - No participants were analyzed; optional MRI assessment was not initiated as the study was stopped.

[4] - No participants were analyzed; optional MRI assessment was not initiated as the study was stopped.

[5] - No participants were analyzed; optional MRI assessment was not initiated as the study was stopped.

[6] - No participants were analyzed; optional MRI assessment was not initiated as the study was stopped.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with anti-BYM338 antibodies

End point title	Number of patients with anti-BYM338 antibodies

End point description:

Investigated the development of immunogenicity against BYM338.

End point type	Secondary

End point timeframe:

end of double-blind treatment (up to 8 months)

End point values	BYM338/bimagrumab 10 mg/kg	BYM338/bimagrumab 3 mg/kg	BYM338/bimagrumab 1 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	40	38	39
Units: Participants	0	1	0	2

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	BYM338 10 mg/kg
Reporting group description: BYM338 10 mg/kg	
Reporting group title	BYM338 3 mg/kg
Reporting group description: BYM338 3 mg/kg	
Reporting group title	BYM338 1 mg/kg
Reporting group description: BYM338 1 mg/kg	
Reporting group title	Placebo
Reporting group description: Placebo	
Reporting group title	Pooled active treatment groups
Reporting group description: Pooled active treatment groups	

Serious adverse events	BYM338 10 mg/kg	BYM338 3 mg/kg	BYM338 1 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 53 (22.64%)	10 / 52 (19.23%)	7 / 51 (13.73%)
number of deaths (all causes)	1	1	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 53 (0.00%)	0 / 52 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer			

subjects affected / exposed	0 / 53 (0.00%)	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bowen's disease			
subjects affected / exposed	0 / 53 (0.00%)	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemangioma			
subjects affected / exposed	1 / 53 (1.89%)	0 / 52 (0.00%)	0 / 51 (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
Skin cancer			
subjects affected / exposed	0 / 53 (0.00%)	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	1 / 53 (1.89%)	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 5	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 / 53 (1.89%)	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Avulsion fracture			
subjects affected / exposed	0 / 53 (0.00%)	0 / 52 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 53 (0.00%)	0 / 52 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			

subjects affected / exposed	0 / 53 (0.00%)	0 / 52 (0.00%)	0 / 51 (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
Hip fracture			
subjects affected / exposed	1 / 53 (1.89%)	0 / 52 (0.00%)	0 / 51 (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
Lower limb fracture			
subjects affected / exposed	1 / 53 (1.89%)	0 / 52 (0.00%)	0 / 51 (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
Patella fracture			
subjects affected / exposed	0 / 53 (0.00%)	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 53 (0.00%)	0 / 52 (0.00%)	0 / 51 (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
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 53 (0.00%)	0 / 52 (0.00%)	0 / 51 (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
Subdural haemorrhage			
subjects affected / exposed	1 / 53 (1.89%)	0 / 52 (0.00%)	0 / 51 (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
Ulna fracture			
subjects affected / exposed	1 / 53 (1.89%)	0 / 52 (0.00%)	0 / 51 (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
Vascular disorders			
Peripheral arterial occlusive disease			

subjects affected / exposed	0 / 53 (0.00%)	0 / 52 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral venous disease			
subjects affected / exposed	0 / 53 (0.00%)	0 / 52 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 53 (1.89%)	0 / 52 (0.00%)	0 / 51 (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
Migraine			
subjects affected / exposed	0 / 53 (0.00%)	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 53 (0.00%)	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 52 (0.00%)	0 / 51 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 52 (0.00%)	0 / 51 (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
Gastrointestinal disorders			
Colitis			

subjects affected / exposed	0 / 53 (0.00%)	0 / 52 (0.00%)	0 / 51 (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
Diarrhoea			
subjects affected / exposed	1 / 53 (1.89%)	0 / 52 (0.00%)	0 / 51 (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
Dysphagia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 52 (0.00%)	0 / 51 (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
Oesophageal achalasia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	1 / 53 (1.89%)	0 / 52 (0.00%)	2 / 51 (3.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 53 (1.89%)	0 / 52 (0.00%)	0 / 51 (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
Respiratory failure			
subjects affected / exposed	1 / 53 (1.89%)	0 / 52 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 53 (0.00%)	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Inclusion body myositis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 52 (0.00%)	0 / 51 (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
Joint effusion			
subjects affected / exposed	1 / 53 (1.89%)	0 / 52 (0.00%)	0 / 51 (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
Mobility decreased			
subjects affected / exposed	0 / 53 (0.00%)	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle haemorrhage			
subjects affected / exposed	0 / 53 (0.00%)	0 / 52 (0.00%)	0 / 51 (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
Rotator cuff syndrome			
subjects affected / exposed	0 / 53 (0.00%)	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 53 (1.89%)	1 / 52 (1.92%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Sepsis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 52 (0.00%)	0 / 51 (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
Urosepsis			

subjects affected / exposed	0 / 53 (0.00%)	0 / 52 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 53 (0.00%)	0 / 52 (0.00%)	0 / 51 (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
Hyperkalaemia			
subjects affected / exposed	1 / 53 (1.89%)	0 / 52 (0.00%)	0 / 51 (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

Serious adverse events	Placebo	Pooled active treatment groups	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 55 (14.55%)	29 / 156 (18.59%)	
number of deaths (all causes)	2	3	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	2 / 55 (3.64%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen's disease			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemangioma			

subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin cancer			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	0 / 55 (0.00%)	2 / 156 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 55 (0.00%)	2 / 156 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Avulsion fracture			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 55 (1.82%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	1 / 55 (1.82%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			

subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	1 / 55 (1.82%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 55 (1.82%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral venous disease			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Headache			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			

subjects affected / exposed	1 / 55 (1.82%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal achalasia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	1 / 55 (1.82%)	3 / 156 (1.92%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 55 (1.82%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inclusion body myositis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint effusion			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Mobility decreased			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle haemorrhage			
subjects affected / exposed	1 / 55 (1.82%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 55 (1.82%)	3 / 156 (1.92%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 2	
Sepsis			
subjects affected / exposed	2 / 55 (3.64%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 55 (1.82%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hyperkalaemia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 156 (0.64%)	
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	BYM338 10 mg/kg	BYM338 3 mg/kg	BYM338 1 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 53 (75.47%)	46 / 52 (88.46%)	38 / 51 (74.51%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	9 / 53 (16.98%)	7 / 52 (13.46%)	12 / 51 (23.53%)
occurrences (all)	10	9	15
Fall			
subjects affected / exposed	30 / 53 (56.60%)	36 / 52 (69.23%)	30 / 51 (58.82%)
occurrences (all)	117	94	73
Foot fracture			
subjects affected / exposed	3 / 53 (5.66%)	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences (all)	3	1	0
Injury			
subjects affected / exposed	3 / 53 (5.66%)	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences (all)	15	1	0
Joint injury			
subjects affected / exposed	3 / 53 (5.66%)	0 / 52 (0.00%)	0 / 51 (0.00%)
occurrences (all)	4	0	0
Laceration			
subjects affected / exposed	1 / 53 (1.89%)	7 / 52 (13.46%)	4 / 51 (7.84%)
occurrences (all)	1	9	5
Ligament sprain			
subjects affected / exposed	5 / 53 (9.43%)	2 / 52 (3.85%)	2 / 51 (3.92%)
occurrences (all)	5	2	2
Limb injury			
subjects affected / exposed	3 / 53 (5.66%)	1 / 52 (1.92%)	1 / 51 (1.96%)
occurrences (all)	3	1	1
Skin abrasion			

subjects affected / exposed	6 / 53 (11.32%)	7 / 52 (13.46%)	4 / 51 (7.84%)
occurrences (all)	10	9	6
Vascular disorders			
Haematoma			
subjects affected / exposed	2 / 53 (3.77%)	0 / 52 (0.00%)	2 / 51 (3.92%)
occurrences (all)	2	0	2
Hypertension			
subjects affected / exposed	5 / 53 (9.43%)	2 / 52 (3.85%)	2 / 51 (3.92%)
occurrences (all)	5	2	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 53 (1.89%)	0 / 52 (0.00%)	0 / 51 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	1 / 53 (1.89%)	2 / 52 (3.85%)	4 / 51 (7.84%)
occurrences (all)	1	2	5
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 53 (0.00%)	0 / 52 (0.00%)	3 / 51 (5.88%)
occurrences (all)	0	0	3
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 53 (0.00%)	4 / 52 (7.69%)	0 / 51 (0.00%)
occurrences (all)	0	5	0
Diarrhoea			
subjects affected / exposed	9 / 53 (16.98%)	5 / 52 (9.62%)	9 / 51 (17.65%)
occurrences (all)	10	8	9
Respiratory, thoracic and mediastinal disorders			
Productive cough			
subjects affected / exposed	0 / 53 (0.00%)	1 / 52 (1.92%)	1 / 51 (1.96%)
occurrences (all)	0	2	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	2 / 53 (3.77%)	1 / 52 (1.92%)	3 / 51 (5.88%)
occurrences (all)	2	2	5
Pruritus			

subjects affected / exposed	3 / 53 (5.66%)	0 / 52 (0.00%)	2 / 51 (3.92%)
occurrences (all)	3	0	2
Rash			
subjects affected / exposed	2 / 53 (3.77%)	3 / 52 (5.77%)	3 / 51 (5.88%)
occurrences (all)	2	5	3
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 53 (1.89%)	5 / 52 (9.62%)	6 / 51 (11.76%)
occurrences (all)	1	6	6
Back pain			
subjects affected / exposed	2 / 53 (3.77%)	4 / 52 (7.69%)	3 / 51 (5.88%)
occurrences (all)	2	4	3
Muscle spasms			
subjects affected / exposed	4 / 53 (7.55%)	8 / 52 (15.38%)	3 / 51 (5.88%)
occurrences (all)	5	9	3
Muscular weakness			
subjects affected / exposed	1 / 53 (1.89%)	3 / 52 (5.77%)	0 / 51 (0.00%)
occurrences (all)	1	4	0
Musculoskeletal chest pain			
subjects affected / exposed	3 / 53 (5.66%)	2 / 52 (3.85%)	0 / 51 (0.00%)
occurrences (all)	3	2	0
Musculoskeletal pain			
subjects affected / exposed	2 / 53 (3.77%)	2 / 52 (3.85%)	4 / 51 (7.84%)
occurrences (all)	2	2	4
Myalgia			
subjects affected / exposed	2 / 53 (3.77%)	4 / 52 (7.69%)	2 / 51 (3.92%)
occurrences (all)	2	4	2
Neck pain			
subjects affected / exposed	0 / 53 (0.00%)	0 / 52 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	1 / 53 (1.89%)	5 / 52 (9.62%)	3 / 51 (5.88%)
occurrences (all)	1	7	5
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	0 / 53 (0.00%)	4 / 52 (7.69%)	1 / 51 (1.96%)
occurrences (all)	0	5	1
Upper respiratory tract infection			
subjects affected / exposed	3 / 53 (5.66%)	3 / 52 (5.77%)	4 / 51 (7.84%)
occurrences (all)	5	4	4

Non-serious adverse events	Placebo	Pooled active treatment groups	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 55 (78.18%)	124 / 156 (79.49%)	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	8 / 55 (14.55%)	28 / 156 (17.95%)	
occurrences (all)	13	34	
Fall			
subjects affected / exposed	34 / 55 (61.82%)	96 / 156 (61.54%)	
occurrences (all)	88	284	
Foot fracture			
subjects affected / exposed	4 / 55 (7.27%)	4 / 156 (2.56%)	
occurrences (all)	4	4	
Injury			
subjects affected / exposed	1 / 55 (1.82%)	4 / 156 (2.56%)	
occurrences (all)	1	16	
Joint injury			
subjects affected / exposed	0 / 55 (0.00%)	3 / 156 (1.92%)	
occurrences (all)	0	4	
Laceration			
subjects affected / exposed	6 / 55 (10.91%)	12 / 156 (7.69%)	
occurrences (all)	8	15	
Ligament sprain			
subjects affected / exposed	3 / 55 (5.45%)	9 / 156 (5.77%)	
occurrences (all)	4	9	
Limb injury			
subjects affected / exposed	0 / 55 (0.00%)	5 / 156 (3.21%)	
occurrences (all)	0	5	
Skin abrasion			

subjects affected / exposed	5 / 55 (9.09%)	17 / 156 (10.90%)	
occurrences (all)	7	25	
Vascular disorders			
Haematoma			
subjects affected / exposed	4 / 55 (7.27%)	4 / 156 (2.56%)	
occurrences (all)	5	4	
Hypertension			
subjects affected / exposed	1 / 55 (1.82%)	9 / 156 (5.77%)	
occurrences (all)	1	9	
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 55 (5.45%)	1 / 156 (0.64%)	
occurrences (all)	3	1	
Headache			
subjects affected / exposed	3 / 55 (5.45%)	7 / 156 (4.49%)	
occurrences (all)	4	8	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 55 (1.82%)	3 / 156 (1.92%)	
occurrences (all)	1	3	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 55 (0.00%)	4 / 156 (2.56%)	
occurrences (all)	0	5	
Diarrhoea			
subjects affected / exposed	5 / 55 (9.09%)	23 / 156 (14.74%)	
occurrences (all)	9	27	
Respiratory, thoracic and mediastinal disorders			
Productive cough			
subjects affected / exposed	3 / 55 (5.45%)	2 / 156 (1.28%)	
occurrences (all)	3	3	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 55 (1.82%)	6 / 156 (3.85%)	
occurrences (all)	1	9	
Pruritus			

subjects affected / exposed	3 / 55 (5.45%)	5 / 156 (3.21%)	
occurrences (all)	3	5	
Rash			
subjects affected / exposed	1 / 55 (1.82%)	8 / 156 (5.13%)	
occurrences (all)	1	10	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 55 (10.91%)	12 / 156 (7.69%)	
occurrences (all)	6	13	
Back pain			
subjects affected / exposed	1 / 55 (1.82%)	9 / 156 (5.77%)	
occurrences (all)	1	9	
Muscle spasms			
subjects affected / exposed	1 / 55 (1.82%)	15 / 156 (9.62%)	
occurrences (all)	1	17	
Muscular weakness			
subjects affected / exposed	3 / 55 (5.45%)	4 / 156 (2.56%)	
occurrences (all)	4	5	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 55 (1.82%)	5 / 156 (3.21%)	
occurrences (all)	1	5	
Musculoskeletal pain			
subjects affected / exposed	2 / 55 (3.64%)	8 / 156 (5.13%)	
occurrences (all)	2	8	
Myalgia			
subjects affected / exposed	0 / 55 (0.00%)	8 / 156 (5.13%)	
occurrences (all)	0	8	
Neck pain			
subjects affected / exposed	5 / 55 (9.09%)	0 / 156 (0.00%)	
occurrences (all)	5	0	
Pain in extremity			
subjects affected / exposed	2 / 55 (3.64%)	9 / 156 (5.77%)	
occurrences (all)	2	13	
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	0 / 55 (0.00%)	5 / 156 (3.21%)	
occurrences (all)	0	6	
Upper respiratory tract infection			
subjects affected / exposed	4 / 55 (7.27%)	10 / 156 (6.41%)	
occurrences (all)	4	13	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 October 2015	Amendment 1 was released before any patients were enrolled. Subsequent to comments received from several Health Authorities, the following changes were made to the protocol and were applicable to the countries as indicated in the amendment: • The protocol was modified to remove reference to patients continuing in the study until commercial availability of bimagrumab, and the duration of Treatment Period 2 was specified as one year. The duration of Treatment Period 2 was to be extended beyond one year in the future if required via a protocol amendment. • The protocol was also amended to clarify that this extension study would be terminated if the outcome of the core study (CBYM338B2203) was negative, i. e., none of the doses of bimagrumab were found to be effective. In the event more than one dose evaluated in the core study was found to be effective, additional data (i.e., from Treatment Period 1 or from other studies of bimagrumab) was to be considered in order to support selection of the dose for Treatment Period 2. • The original protocol described that the study could be terminated by the Sponsor at any time and for any reason. In response to Health Authority feedback, it was proposed to include additional text to account for the possibility that the trial was to be terminated as per protocol in case the benefit/risk of bimagrumab becomes negative or if the DMC made a recommendation to stop this extension study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The core study has been completed but since the core study did not meet the primary end point, the extension study was terminated as per protocol.

Notes: