Clinical trial results:
A 28 week, randomized, double-blind, placebo-controlled, two-part, multi-center,parallel group dose range finding study to assess the effect of monthly doses of bimagrumab 70, 210, and 700 mg on skeletal muscle strength and function in older adults with sarcopenia (InvestiGAIT)

Summary

EudraCT number	2014-003482-25
Trial protocol	ES DK BE CZ
Global end of trial date	28 June 2018

Results information

Result version number	v1 (current)
This version publication date	30 June 2019
First version publication date	30 June 2019

Trial information

Trial identification

Sponsor protocol code	CBYM338E2202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02333331
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, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.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	Final
Date of interim/final analysis	28 June 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the effect of 24 weeks of bimagrumab treatment on patient physical function assessed by a change in the SPPB total score from baseline to week 25 relative to placebo in older adults with sarcopenia.

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	09 December 2014
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: 3
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Czech Republic: 1
Country: Number of subjects enrolled	Denmark: 8
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Japan: 22
Country: Number of subjects enrolled	Russian Federation: 19
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Korea, Republic of: 7
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	Taiwan: 7
Country: Number of subjects enrolled	United States: 135
Worldwide total number of subjects	217
EEA total number of subjects	22

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)	0
From 65 to 84 years	189
85 years and over	28

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 220 patients were randomized to receive six doses of either BYM338 70 mg, BYM338 210 mg, BYM338 700 mg or the placebo. However, only 217 patients were dosed with BYM338 or placebo due to the withdrawal of three patients who did not meet the inclusion/exclusion criteria prior to receiving the first dose.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	BYM338 70 mg

Arm description:

BYM338 70 mg intravenous infusion

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:

Bimagrumab 70 mg intravenous (i.v.) infusion every 4 weeks for 24-week treatment period

Arm title	BYM338 210 mg

Arm description:

BYM338 210 mg intravenous infusion

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:

Bimagrumab 210 mg intravenous (i.v.) infusion every 4 weeks for 24-week treatment period

Arm title	BYM338 700 mg

Arm description:

BYM338 700 mg intravenous infusion

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:
Bimagrumab 700 mg intravenous (i.v.) infusion every 4 weeks for 24-week treatment period

Arm title	Placebo
Arm description: Placebo intravenous infusion	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	BYM338
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
Placebo intravenous (i.v.) infusion every 4 weeks for 24-week treatment period

Number of subjects in period 1	BYM338 70 mg	BYM338 210 mg	BYM338 700 mg
Started	19	18	113
Completed	17	12	95
Not completed	2	6	18
Adverse event, serious fatal	-	-	2
Physician decision	-	1	-
Adverse event, non-fatal	1	-	4
Patient/Guardian Decision	1	2	9
Protocol Deviation	-	3	2
Lost to follow-up	-	-	1

Number of subjects in period 1	Placebo
Started	67
Completed	64
Not completed	3
Adverse event, serious fatal	-
Physician decision	-
Adverse event, non-fatal	1
Patient/Guardian Decision	1
Protocol Deviation	1
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	BYM338 70 mg
Reporting group description: BYM338 70 mg intravenous infusion	
Reporting group title	BYM338 210 mg
Reporting group description: BYM338 210 mg intravenous infusion	
Reporting group title	BYM338 700 mg
Reporting group description: BYM338 700 mg intravenous infusion	
Reporting group title	Placebo
Reporting group description: Placebo intravenous infusion	

Reporting group values	BYM338 70 mg	BYM338 210 mg	BYM338 700 mg
Number of subjects	19	18	113
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)	0	0	0
From 65-84 years	15	15	101
85 years and over	4	3	12
Age Continuous Units: years			
arithmetic mean	79.3	78.0	79.5
standard deviation	± 5.89	± 6.38	± 5.46
Sex: Female, Male Units: Subjects			
Female	9	8	66
Male	10	10	47
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	5	3	17
Native Hawaiian or Other Pacific Islander	0	0	1
Black or African American	3	0	0
White	11	14	93
More than one race	0	0	0
Unknown or Not Reported	0	1	1

Reporting group values	Placebo	Total	
Number of subjects	67	217	
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)	0	0	
From 65-84 years	58	189	
85 years and over	9	28	
Age Continuous Units: years			
arithmetic mean	78.3		
standard deviation	± 5.03	-	
Sex: Female, Male Units: Subjects			
Female	43	126	
Male	24	91	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	
Asian	11	36	
Native Hawaiian or Other Pacific Islander	0	1	
Black or African American	1	4	
White	54	172	
More than one race	1	1	
Unknown or Not Reported	0	2	

End points

End points reporting groups	
Reporting group title	BYM338 70 mg
Reporting group description: BYM338 70 mg intravenous infusion	
Reporting group title	BYM338 210 mg
Reporting group description: BYM338 210 mg intravenous infusion	
Reporting group title	BYM338 700 mg
Reporting group description: BYM338 700 mg intravenous infusion	
Reporting group title	Placebo
Reporting group description: Placebo intravenous infusion	

Primary: Change from Baseline in total Short Physical Performance Battery (SPPB) Score to week 25

End point title	Change from Baseline in total Short Physical Performance Battery (SPPB) Score to week 25

End point description:

Change from Baseline in total Short Physical Performance Battery (SPPB) Score to week 25; SPPB is a series of six activities involving three domains of physical function – balance, usual walking speed and rising from a chair , is commonly used globally to assess and quantify (score 0-12) lower extremity function and has been shown to predict future adverse health events. A decline of one or more points in the SPPB total score is predictive of a decrease in lower extremity function and future adverse clinical outcomes in older adults, including falls, hospitalizations, institutionalization, incident disability and death

End point type	Primary

End point timeframe:

Baseline, week 25

End point values	BYM338 70 mg	BYM338 210 mg	BYM338 700 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	18	113	67
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	7.1 (± 2.12)	7.3 (± 2.11)	7.2 (± 1.63)	7.3 (± 1.67)
Week 25	8.5 (± 2.48)	8.7 (± 1.64)	8.7 (± 2.12)	8.4 (± 2.25)

Statistical analyses

Statistical analysis title	Change from Baseline in total SPPB Score WK 25
Comparison groups	Placebo v BYM338 70 mg

Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.274
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.64
upper limit	1.21

Statistical analysis title	Change from Baseline in total SPPB Score WK 25
Comparison groups	BYM338 210 mg v Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.32
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.83
upper limit	1.35

Statistical analysis title	Change from Baseline in total SPPB Score WK 25
Comparison groups	BYM338 700 mg v Placebo
Number of subjects included in analysis	180
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.134
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	0.87

Secondary: Change from Baseline at Week 25 in the 6 minute walk test (6MWT)

distance	
End point title	Change from Baseline at Week 25 in the 6 minute walk test (6MWT) distance
End point description:	
Change from Baseline at Week 25 in the 6 minute walk test (6MWT) distance to measure improvement in physical function	
End point type	Secondary
End point timeframe:	
Baseline, week 25	

End point values	BYM338 70 mg	BYM338 210 mg	BYM338 700 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	18	113	67
Units: meters				
arithmetic mean (standard deviation)				
Baseline	293.30 (± 91.842)	291.81 (± 82.527)	294.30 (± 83.602)	312.43 (± 93.924)
Week 25	304.98 (± 102.934)	340.71 (± 72.911)	315.32 (± 97.020)	322.71 (± 103.865)

Statistical analyses

Statistical analysis title	Change from Baseline in 6MWT WK 25
Comparison groups	BYM338 70 mg v Placebo
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.576
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-3.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.6
upper limit	30.95

Statistical analysis title	Change from Baseline in 6MWT WK 25
Comparison groups	BYM338 210 mg v Placebo

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.178
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	19.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.2
upper limit	61.41

Statistical analysis title	Change from Baseline in 6MWT WK 25
Comparison groups	BYM338 700 mg v Placebo
Number of subjects included in analysis	180
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.163
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	10.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.4
upper limit	30.98

Secondary: Change from Baseline to Week 25 in usual Gait speed (GS) over 4 meters

End point title	Change from Baseline to Week 25 in usual Gait speed (GS) over 4 meters

End point description:

Change from Baseline to Week 25 in usual Gait speed (GS) over 4 meters Gait speed in this study was assessed as part of the SPPB, over a 4 meter distance of a 6 meter course. This test assessed a person’s usual walking speed, which was defined as the speed a person normally walks from one place to another without urgency (e.g., walking down a hallway).

End point type	Secondary

End point timeframe:

baseline, week 25

End point values	BYM338 70 mg	BYM338 210 mg	BYM338 700 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	18	113	67
Units: m/sec				
arithmetic mean (standard deviation)				
Baseline	2.37 (± 0.684)	2.72 (± 0.752)	2.58 (± 0.624)	2.70 (± 0.493)
Week 25	3.12 (± 0.857)	3.60 (± 0.699)	3.30 (± 0.902)	3.23 (± 0.838)

Statistical analyses

Statistical analysis title	Change from Baseline in GS over 4 meters WK 25
Comparison groups	BYM338 70 mg v Placebo
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.488
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.1

Statistical analysis title	Change from Baseline in GS over 4 meters WK 25
Comparison groups	BYM338 210 mg v Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.055
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.22

Statistical analysis title	Change from Baseline in GS over 4 meters WK 25
Comparison groups	BYM338 700 mg v Placebo

Number of subjects included in analysis	180
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.161
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.09

Secondary: Percentage Change from Baseline to Week 25 on appendicular skeletal muscle index (ASMI) measured by Dual Energy X-ray Absorptiometry (DXA)

End point title	Percentage Change from Baseline to Week 25 on appendicular skeletal muscle index (ASMI) measured by Dual Energy X-ray Absorptiometry (DXA)

End point description:

Change from Baseline to Week 25 on appendicular skeletal muscle index (ASMI) measured by Dual Energy X-ray Absorptiometry (DXA) Appendicular skeletal muscle index (ASMI) is a core requirement for determining the presence of sarcopenia and is calculated as the sum of the appendicular lean mass (kg) of the two upper and two lower limbs quantified by DXA, divided by height (m2). Therefore, an increase in ASMI indicates an increase in the quantity of an individual's lean mass.

End point type	Secondary

End point timeframe:

baseline, week 25

End point values	BYM338 70 mg	BYM338 210 mg	BYM338 700 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	18	113	67
Units: kg/m2				
arithmetic mean (standard deviation)				
Baseline	5.99 (± 0.886)	5.87 (± 0.795)	5.70 (± 0.823)	5.55 (± 0.753)
Week 25	6.04 (± 0.947)	6.42 (± 0.849)	6.10 (± 0.836)	5.60 (± 0.717)

Statistical analyses

Statistical analysis title	Change from Baseline of ASMI measured by DXA WK 25
Comparison groups	BYM338 70 mg v Placebo

Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.213
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.03

Statistical analysis title	Change from Baseline of ASMI measured by DXA WK 25
Comparison groups	BYM338 210 mg v Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	1.09

Statistical analysis title	Change from Baseline of ASMI measured by DXA WK 25
Comparison groups	BYM338 700 mg v Placebo
Number of subjects included in analysis	180
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	1.08

Secondary: Percentage Change from Baseline to Week 25 on Total lean body mass

measured by Dual Energy X-ray Absorptiometry (DXA)	
End point title	Percentage Change from Baseline to Week 25 on Total lean body mass measured by Dual Energy X-ray Absorptiometry (DXA)

End point description:

Change from Baseline to Week 25 on Total lean body mass measured by Dual Energy X-ray Absorptiometry (DXA) total lean body mass (LBM) is measured by dual energy x-ray absorptiometry (DXA).Percent Change = [(LBM at Visit - LBM at Baseline) / LBM at Baseline] * 100.

End point type	Secondary

End point timeframe:

baseline, week 25

End point values	BYM338 70 mg	BYM338 210 mg	BYM338 700 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	18	113	67
Units: kg				
arithmetic mean (standard deviation)				
Baseline	37.44 (± 8.507)	35.84 (± 7.300)	35.39 (± 8.891)	33.65 (± 6.890)
Week 25	38.26 (± 8.660)	39.52 (± 8.343)	37.86 (± 9.064)	33.95 (± 6.921)

Statistical analyses

Statistical analysis title	Change from Baseline of Total Lean Body Mass WK 25
Comparison groups	BYM338 70 mg v Placebo
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.458
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.02

Statistical analysis title	Change from Baseline of Total Lean Body Mass WK 25
Comparison groups	BYM338 210 mg v Placebo

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	1.08

Statistical analysis title	Change from Baseline of Total Lean Body Mass WK 25
Comparison groups	BYM338 700 mg v Placebo
Number of subjects included in analysis	180
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	1.07

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	BYM338 70 mg
Reporting group description: BYM338 70 mg	
Reporting group title	BYM338 210 mg
Reporting group description: BYM338 210 mg	
Reporting group title	BYM338 700 mg
Reporting group description: BYM338 700 mg	
Reporting group title	Placebo
Reporting group description: Placebo	

Serious adverse events	BYM338 70 mg	BYM338 210 mg	BYM338 700 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	3 / 18 (16.67%)	14 / 113 (12.39%)
number of deaths (all causes)	0	0	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to lung			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 113 (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
Renal neoplasm			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 113 (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
Vascular disorders			

Hypertension			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 113 (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
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory arrest			

subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	0 / 113 (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
Hepatic enzyme increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Aortic injury			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
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 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	0 / 113 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac failure congestive			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardio-respiratory arrest			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Myocardial infarction			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	0 / 113 (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
Pulseless electrical activity			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Syncope			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Colitis ulcerative			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 113 (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 disorder			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 113 (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
Myalgia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 113 (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
Infections and infestations			
Erysipelas			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 113 (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
Pneumonia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
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			
Decreased appetite			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 67 (7.46%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to lung			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal neoplasm			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			

Anaphylactic reaction				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory arrest				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Blood alkaline phosphatase increased				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic enzyme increased				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Aortic injury				

subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal fracture				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial fibrillation				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory arrest				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulseless electrical activity				

subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorder			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Myalgia			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neck pain			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Erysipelas			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	BYM338 70 mg	BYM338 210 mg	BYM338 700 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 19 (63.16%)	13 / 18 (72.22%)	94 / 113 (83.19%)
Vascular disorders			
Hypertension			

subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	9 / 113 (7.96%)
occurrences (all)	0	1	13
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	1 / 19 (5.26%)	1 / 18 (5.56%)	5 / 113 (4.42%)
occurrences (all)	1	1	6
Infusion site swelling			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	0 / 113 (0.00%)
occurrences (all)	0	2	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	1 / 113 (0.88%)
occurrences (all)	0	1	1
Oedema			
subjects affected / exposed	1 / 19 (5.26%)	1 / 18 (5.56%)	0 / 113 (0.00%)
occurrences (all)	1	1	0
Peripheral swelling			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	4 / 113 (3.54%)
occurrences (all)	0	0	4
Productive cough			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences (all)	1	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	0 / 113 (0.00%)
occurrences (all)	0	1	0

Investigations			
Amylase increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	4 / 113 (3.54%)
occurrences (all)	0	0	4
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	3 / 113 (2.65%)
occurrences (all)	1	0	3
C-reactive protein increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Lipase increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	6 / 113 (5.31%)
occurrences (all)	0	0	7
Liver function test increased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	1 / 113 (0.88%)
occurrences (all)	0	1	1
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	1 / 113 (0.88%)
occurrences (all)	0	2	1
Contusion			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	5 / 113 (4.42%)
occurrences (all)	0	1	7
Fall			
subjects affected / exposed	2 / 19 (10.53%)	3 / 18 (16.67%)	28 / 113 (24.78%)
occurrences (all)	6	4	38
Muscle strain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	2 / 113 (1.77%)
occurrences (all)	0	1	2
Skin abrasion			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences (all)	1	0	1
Wound			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			

Bradycardia			
subjects affected / exposed	2 / 19 (10.53%)	0 / 18 (0.00%)	3 / 113 (2.65%)
occurrences (all)	2	0	3
Palpitations			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	2 / 113 (1.77%)
occurrences (all)	0	1	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	6 / 113 (5.31%)
occurrences (all)	0	0	7
Dysgeusia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	4 / 113 (3.54%)
occurrences (all)	0	1	4
Headache			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	5 / 113 (4.42%)
occurrences (all)	0	0	5
Hypoaesthesia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Muscle contractions involuntary			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	3 / 113 (2.65%)
occurrences (all)	1	0	3
Presyncope			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences (all)	1	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	3 / 113 (2.65%)
occurrences (all)	0	1	3
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 19 (10.53%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences (all)	2	0	1
Eye disorders			
Trichiasis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0

Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	6 / 113 (5.31%)
occurrences (all)	0	1	6
Dental necrosis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	1 / 19 (5.26%)	3 / 18 (16.67%)	22 / 113 (19.47%)
occurrences (all)	2	5	28
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	8 / 113 (7.08%)
occurrences (all)	0	0	9
Toothache			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	4 / 113 (3.54%)
occurrences (all)	0	0	7
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 19 (0.00%)	3 / 18 (16.67%)	3 / 113 (2.65%)
occurrences (all)	0	3	3
Actinic keratosis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Dermatitis contact			

subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	2 / 113 (1.77%)
occurrences (all)	1	0	2
Eczema asteatotic			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	2 / 113 (1.77%)
occurrences (all)	0	1	2
Rash			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	5 / 113 (4.42%)
occurrences (all)	0	0	7
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Skin fissures			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	1 / 113 (0.88%)
occurrences (all)	0	1	1
Renal and urinary disorders			
Lower urinary tract symptoms			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Nocturia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences (all)	1	0	1
Endocrine disorders			
Androgen deficiency			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	1 / 113 (0.88%)
occurrences (all)	0	2	1
Back pain			
subjects affected / exposed	1 / 19 (5.26%)	2 / 18 (11.11%)	5 / 113 (4.42%)
occurrences (all)	1	2	5
Muscle spasms			
subjects affected / exposed	4 / 19 (21.05%)	5 / 18 (27.78%)	37 / 113 (32.74%)
occurrences (all)	6	7	50
Musculoskeletal pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	2 / 113 (1.77%)
occurrences (all)	1	0	2
Myalgia			
subjects affected / exposed	1 / 19 (5.26%)	1 / 18 (5.56%)	3 / 113 (2.65%)
occurrences (all)	1	2	3
Osteoarthritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	4 / 113 (3.54%)
occurrences (all)	0	0	4
Pain in extremity			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	6 / 113 (5.31%)
occurrences (all)	0	1	7
Plantar fasciitis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	6 / 113 (5.31%)
occurrences (all)	1	0	7
Fungal skin infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Gingivitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			

subjects affected / exposed	3 / 19 (15.79%)	1 / 18 (5.56%)	5 / 113 (4.42%)
occurrences (all)	4	1	6
Periodontitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	1 / 113 (0.88%)
occurrences (all)	1	0	2
Sinusitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	4 / 113 (3.54%)
occurrences (all)	0	0	5
Upper respiratory tract infection			
subjects affected / exposed	1 / 19 (5.26%)	2 / 18 (11.11%)	5 / 113 (4.42%)
occurrences (all)	1	2	5
Urinary tract infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	6 / 113 (5.31%)
occurrences (all)	1	0	6
Vaginal infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Viral infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	5 / 113 (4.42%)
occurrences (all)	0	0	5
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 19 (5.26%)	1 / 18 (5.56%)	5 / 113 (4.42%)
occurrences (all)	1	1	6
Hyperglycaemia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	2 / 113 (1.77%)
occurrences (all)	0	1	2

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 67 (61.19%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 67 (5.97%)		
occurrences (all)	5		
General disorders and administration site conditions			

Chest discomfort subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Fatigue subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Infusion site swelling subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Non-cardiac chest pain subjects affected / exposed occurrences (all)	1 / 67 (1.49%) 1		
Oedema subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Peripheral swelling subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Productive cough subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Product issues Device dislocation subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Investigations Amylase increased			

subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences (all)	1		
C-reactive protein increased			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences (all)	1		
Lipase increased			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Liver function test increased			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	7 / 67 (10.45%)		
occurrences (all)	8		
Fall			
subjects affected / exposed	24 / 67 (35.82%)		
occurrences (all)	46		
Muscle strain			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Skin abrasion			
subjects affected / exposed	2 / 67 (2.99%)		
occurrences (all)	2		
Wound			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Cardiac disorders			

Bradycardia subjects affected / exposed occurrences (all) Palpitations subjects affected / exposed occurrences (all)	 0 / 67 (0.00%) 0 0 / 67 (0.00%) 0		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Dysgeusia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Hypoaesthesia subjects affected / exposed occurrences (all) Muscle contractions involuntary subjects affected / exposed occurrences (all) Presyncope subjects affected / exposed occurrences (all)	 0 / 67 (0.00%) 0 0 / 67 (0.00%) 0 3 / 67 (4.48%) 3 0 / 67 (0.00%) 0 0 / 67 (0.00%) 0 0 / 67 (0.00%) 0		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	 0 / 67 (0.00%) 0		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	 2 / 67 (2.99%) 2		
Eye disorders Trichiasis subjects affected / exposed occurrences (all)	 0 / 67 (0.00%) 0		

Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences (all)	1		
Dental necrosis			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	2 / 67 (2.99%)		
occurrences (all)	2		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences (all)	1		
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Actinic keratosis			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Dermatitis contact			

subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Eczema subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Eczema asteatotic subjects affected / exposed occurrences (all)	1 / 67 (1.49%) 1		
Pruritus subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Rash subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Seborrhoeic dermatitis subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Skin fissures subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Urticaria subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Renal and urinary disorders			
Lower urinary tract symptoms subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Nocturia subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Endocrine disorders			
Androgen deficiency subjects affected / exposed occurrences (all)	0 / 67 (0.00%) 0		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	2 / 67 (2.99%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	3 / 67 (4.48%)		
occurrences (all)	3		
Muscle spasms			
subjects affected / exposed	10 / 67 (14.93%)		
occurrences (all)	12		
Musculoskeletal pain			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	2 / 67 (2.99%)		
occurrences (all)	2		
Osteoarthritis			
subjects affected / exposed	2 / 67 (2.99%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	3 / 67 (4.48%)		
occurrences (all)	4		
Plantar fasciitis			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 67 (2.99%)		
occurrences (all)	2		
Fungal skin infection			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Gingivitis			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			

subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Periodontitis			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	5 / 67 (7.46%)		
occurrences (all)	5		
Urinary tract infection			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences (all)	1		
Vaginal infection			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Viral infection			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 May 2015	Amendment 1:The purpose of this amendment was to correct minor inconsistencies identified during health authority and ethics committee reviews, and to provide some clarifications on study assessments. At the time of implementing this amendment, 3 patients had begun treatment; none were affected by changes made to the protocol. The changes described in this amendment did not affect the objectives of the study, impact the safety of the patients or change the analysis of the study data. Some adjustments were made to the inclusion and exclusion criteria as a result of experience with the population required for this study.
06 September 2016	Amendment 2: The purpose of this amendment is to align the study design and endpoints with progress made in the field of sarcopenia and the bimagrumab program since the original protocol was submitted, integrate new safety data from recently completed bimagrumab studies, facilitate recruitment, and reduce patient and site burden where possible.
04 October 2017	Amendment 3: The primary purpose of this amendment was to present a new safety observation and the resultant modifications to the protocol, and to adjust the sample size to enable program decision making at the completion of Part A. In addition, editorial revisions were made to clarify the terminology of the oral nutritional supplement and to improve understanding in other areas of the text.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported