



Clinical trial results:

A randomized, double-blind, placebo-controlled, multi-center study of BYM338 for treatment of cachexia in patients with stage IV non-small cell lung cancer or stage III/IV adenocarcinoma of the pancreas

Summary

EudraCT number	2010-024342-30
Trial protocol	GB LT
Global end of trial date	24 April 2014

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	16 August 2015

Trial information

Trial identification

Sponsor protocol code	CBYM338X2202
-----------------------	--------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01433263
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	24 April 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 April 2014
Global end of trial reached?	Yes
Global end of trial date	24 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the preliminary efficacy of a single intravenous i.v. dose of BYM338 in increasing thigh muscle volume (TMV) as assessed by Magnetic Resonance Imaging (MRI) compared to placebo.

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	22 August 2011
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	United States: 24
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	Switzerland: 10
Country: Number of subjects enrolled	Lithuania: 3
Country: Number of subjects enrolled	Romania: 13
Worldwide total number of subjects	57
EEA total number of subjects	23

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)	57
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Core Phase single dose BYM338 30mg/kg i.v. active or placebo with 8week followup. Followup phase started Week 8 & patients on placebo in the Core Phase were given BYM338 & patients on BYM338 in Core Phase continued to be followed for an additional 8 weeks. Late BYM338 are patients who received Placebo during Core Phase and then BYM338 after Week 8.

Pre-assignment

Screening details:

Core Phase single dose BYM338 30mg/kg i.v. active or placebo with 8week followup. Followup phase started Week 8 & patients on placebo in the Core Phase were given BYM338 & patients on BYM338 in Core Phase continued to be followed for an additional 8 weeks. Late BYM338 are patients who received Placebo during Core Phase and then BYM338 after Week 8.

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, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	30mg/kg BYM338

Arm description: -

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

Dosage and administration details:

single dose BYM338 30 mg/kg i.v. lyophilized powder for injection

Arm title	Placebo / late 30mg/kg BYM338
------------------	-------------------------------

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo to match BYM338
Investigational medicinal product code	BYM338
Other name	Placebo
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

single dose Placebo to match BYM338 i.v.

Number of subjects in period 1	30mg/kg BYM338	Placebo / late 30mg/kg BYM338
Started	29	28
Completed	10	16
Not completed	19	12
Adverse event, serious fatal	5	3
Consent withdrawn by subject	10	7
Adverse event, non-fatal	3	1
Protocol Deviation	1	-
Lost to follow-up	-	1

Baseline characteristics

Reporting groups

Reporting group title	30mg/kg BYM338
Reporting group description: -	
Reporting group title	Placebo / late 30mg/kg BYM338
Reporting group description: -	

Reporting group values	30mg/kg BYM338	Placebo / late 30mg/kg BYM338	Total
Number of subjects	29	28	57
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)	17	14	31
From 65-84 years	12	14	26
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	62.8	61.5	
standard deviation	± 10.17	± 10.74	-
Gender, Male/Female Units: participants			
Male	20	22	42
Female	9	6	15

End points

End points reporting groups

Reporting group title	30mg/kg BYM338
Reporting group description: -	
Reporting group title	Placebo / late 30mg/kg BYM338
Reporting group description: -	

Primary: Percentage Change from Baseline of Thigh Muscle Volume (TMV) by MRI Scan at week 8

End point title	Percentage Change from Baseline of Thigh Muscle Volume (TMV) by MRI Scan at week 8
End point description:	Thigh Muscle Volume (TMV) change was evaluated by a responder analysis. Patients whose loss of muscle TMV by MRI was no more than or equal to 2% at Week 8 was considered responders.
End point type	Primary
End point timeframe:	Baseline, week 8

End point values	30mg/kg BYM338	Placebo / late 30mg/kg BYM338		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	22		
Units: Percentage Change of TMV				
arithmetic mean (standard deviation)	2 (± 8.094)	0.65 (± 8.239)		

Statistical analyses

Statistical analysis title	% Change from Baseline of TMV by MRI Scan week 8
Comparison groups	30mg/kg BYM338 v Placebo / late 30mg/kg BYM338
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.541
Method	ANCOVA

Secondary: Percentage Change in body weight from baseline at week 7 and week 9

End point title	Percentage Change in body weight from baseline at week 7 and week 9
End point description:	Percentage Change in body weight from baseline in kilograms (kg) at week 7 and week 9

End point type	Secondary
End point timeframe:	
Baseline, Week 7 and Week 9	

End point values	30mg/kg BYM338	Placebo / late 30mg/kg BYM338		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	28		
Units: Percent Change of Weight (kg)				
arithmetic mean (standard deviation)				
Week 7 (n= 15, 17)	-3.3 (± 5.035)	-0.68 (± 4.457)		
Week 9 (n=14,16)	-1.8 (± 7.131)	-0.32 (± 3.271)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Serum Concentration (Cmax)

End point title	Maximum Observed Serum Concentration (Cmax)
End point description:	
Blood samples for pharmacokinetic (PK) evaluation were drawn on Day 1 30mg/kg BYM338 (Core) or week 8 Late 30mg/kg BYM338 (when placebo subjects were rolled over to active). PK parameters were calculated from plasma concentration-time data using non-compartmental methods.	
End point type	Secondary
End point timeframe:	
Day 1 and Week 8	

End point values	30mg/kg BYM338	Placebo / late 30mg/kg BYM338		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	14		
Units: ng/ml				
arithmetic mean (standard deviation)	422 (± 142)	408 (± 78.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach the Maximum Concentration After Drug Administration (Tmax)

End point title	Time to Reach the Maximum Concentration After Drug Administration (Tmax)
End point description: Blood samples for pharmacokinetic (PK) evaluation were drawn on Day 1 30mg/kg BYM338 (Core) or week 8 Late 30mg/kg BYM338 (when placebo subjects were rolled over to active). Tmax was directly determined from the raw serum concentration-time data.	
End point type	Secondary
End point timeframe: Day 1 and Week 8	

End point values	30mg/kg BYM338	Placebo / late 30mg/kg BYM338		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	14		
Units: hr				
median (inter-quartile range (Q1-Q3))	2.05 (1.83 to 3.92)	2.22 (2 to 4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change from Baseline in total lean body mass (LBM) by Dual-Energy X-ray Absorptiometry (DXA) compared to placebo: at week 8

End point title	Percentage Change from Baseline in total lean body mass (LBM) by Dual-Energy X-ray Absorptiometry (DXA) compared to placebo: at week 8
End point description: total lean body mass (LBM) is measured by dual energy x-ray absorptiometry (DXA). Percent Change = $[(\text{LBM at Visit} - \text{LBM at Baseline}) / \text{LBM at Baseline}] * 100$.	
End point type	Secondary
End point timeframe: Baseline, Week 8	

End point values	30mg/kg BYM338	Placebo / late 30mg/kg BYM338		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	22		
Units: Percentage Change in LBM				
arithmetic mean (standard deviation)	4.97 (\pm 7.537)	2.41 (\pm 4.625)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change from Baseline of Bone Mineral Density (BMD) by Dual-Energy X-ray Absorptiometry (DXA) compared to placebo at week 8

End point title	Percentage Change from Baseline of Bone Mineral Density (BMD) by Dual-Energy X-ray Absorptiometry (DXA) compared to placebo at week 8
-----------------	---

End point description:

Bone Mineral Density (BMD) is measured by dual energy x-ray absorptiometry (DXA). Percent Change = $[(\text{BMD at Visit} - \text{BMD at Baseline}) / \text{BMD at Baseline}] * 100$.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline, Week 8

End point values	30mg/kg BYM338	Placebo / late 30mg/kg BYM338		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	22		
Units: Percentage Change in BMD				
arithmetic mean (standard deviation)	0.51 (± 3.712)	0.14 (± 4.14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change from Baseline of physical activity levels (using the ActivPAL™ device) number of steps taken compared to placebo at week 4 and 7

End point title	Percentage Change from Baseline of physical activity levels (using the ActivPAL™ device) number of steps taken compared to placebo at week 4 and 7
-----------------	--

End point description:

Each patient was required to wear the ActivPal™ for a span of 6 days at Week 4 and Week 7 for patient home activity recording. The ActivPal™ was given to patients in clinic to wear for 6 consecutive days. The ActivPAL™ records periods spent sitting, standing and walking, sit-to-stand transitions, step count and rate of stepping (cadence) over a maximum period of 10 days with a fully charged new battery.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline, Week 4 and Week 7

End point values	30mg/kg BYM338	Placebo / late 30mg/kg BYM338		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	28		
Units: percentage change in number of steps				

arithmetic mean (standard deviation)				
Week 4 (n=18, 23)	917.78 (± 3720.491)	63.59 (± 130.913)		
Week 7 (n=13, 22)	-17.37 (± 80.35)	35.8 (± 119.486)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change from Baseline of physical activity levels (using the ActivPAL™ device) Time Sedentary taken compared to placebo at week 4 and 7

End point title	Percentage Change from Baseline of physical activity levels (using the ActivPAL™ device) Time Sedentary taken compared to placebo at week 4 and 7
End point description:	Each patient was required to wear the ActivPal™ for a span of 6 days at Week 4 and Week 7 for patient home activity recording. The ActivPal™ was given to patients in clinic to wear for 6 consecutive days. The ActivPAL™ records periods spent sitting, standing and walking, sit-to-stand transitions, step count and rate of stepping (cadence) over a maximum period of 10 days with a fully charged new battery.
End point type	Secondary
End point timeframe:	Baseline, Week 4 and Week 7

End point values	30mg/kg BYM338	Placebo / late 30mg/kg BYM338		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	28		
Units: percentage change in time (minutes)				
arithmetic mean (standard deviation)				
Week 4 (n=18, 23)	-0.05 (± 10.049)	52.25 (± 207.403)		
Week 7 (n=13, 22)	107.85 (± 280.791)	60.25 (± 222.366)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change from Baseline of physical activity levels (using the ActivPAL™ device) Time Standing compared to placebo at week 4 and 7

End point title	Percentage Change from Baseline of physical activity levels (using the ActivPAL™ device) Time Standing compared to placebo at week 4 and 7
End point description:	Each patient was required to wear the ActivPal™ for a span of 6 days at Week 4 and Week 7 for patient home activity recording. The ActivPal™ was given to patients in clinic to wear for 6 consecutive days.

The ActivPAL™ records periods spent sitting, standing and walking, sit-to-stand transitions, step count and rate of stepping (cadence) over a maximum period of 10 days with a fully charged new battery.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline, Week 4 and Week 7

End point values	30mg/kg BYM338	Placebo / late 30mg/kg BYM338		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	28		
Units: percentage change in time (minutes)				
arithmetic mean (standard deviation)				
Week 4 (n=18, 23)	1.82 (± 78.364)	38.17 (± 111.361)		
Week 7 (n=13, 22)	41.9 (± 251.291)	23.76 (± 99.268)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change from Baseline of physical activity levels (using the ActivPAL™ device) Time Stepping compared to placebo at week 4 and 7

End point title	Percentage Change from Baseline of physical activity levels (using the ActivPAL™ device) Time Stepping compared to placebo at week 4 and 7
-----------------	--

End point description:

Each patient was required to wear the ActivPal™ for a span of 6 days at Week 4 and Week 7 for patient home activity recording. The ActivPal™ was given to patients in clinic to wear for 6 consecutive days. The ActivPAL™ records periods spent sitting, standing and walking, sit-to-stand transitions, step count and rate of stepping (cadence) over a maximum period of 10 days with a fully charged new battery.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline, Week 4 and Week 7

End point values	30mg/kg BYM338	Placebo / late 30mg/kg BYM338		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	28		
Units: percentage change in time (minutes)				
arithmetic mean (standard deviation)				
Week 4 (n=18, 22)	1446.69 (± 6011.324)	85.3 (± 159.949)		
Week 7 (n=13, 21)	-31.64 (± 67.18)	33.39 (± 129.218)		

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 are reported in this record from 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	16.1
--------------------	------

Reporting groups

Reporting group title	Core - 30 mg/kg BYM338
-----------------------	------------------------

Reporting group description:

Core - 30 mg/kg BYM338

Reporting group title	Core - Placebo
-----------------------	----------------

Reporting group description:

Core - Placebo

Reporting group title	Follow-up - 30 mg/kg BYM338
-----------------------	-----------------------------

Reporting group description:

Follow-up - 30 mg/kg BYM338

Reporting group title	Follow-up - Placebo
-----------------------	---------------------

Reporting group description:

Follow-up - Placebo

Reporting group title	Follow-up - 30mg/kg BYM338 Late
-----------------------	---------------------------------

Reporting group description:

Follow-up - 30mg/kg BYM338 Late

Serious adverse events	Core - 30 mg/kg BYM338	Core - Placebo	Follow-up - 30 mg/kg BYM338
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 29 (62.07%)	4 / 28 (14.29%)	7 / 19 (36.84%)
number of deaths (all causes)	6	1	4
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	0 / 19 (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
Malignant neoplasm progression			

subjects affected / exposed	6 / 29 (20.69%)	0 / 28 (0.00%)	3 / 19 (15.79%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 4	0 / 0	0 / 2
Metastases to central nervous system			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Pancreatic carcinoma			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	0 / 19 (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
Tumour pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 29 (6.90%)	0 / 28 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angiopathy			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Peripheral ischaemia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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

Disease progression			
subjects affected / exposed	0 / 29 (0.00%)	1 / 28 (3.57%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Oedema peripheral			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Dyspnoea			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Haemoptysis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	0 / 19 (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 aspiration			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Pneumothorax			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pulmonary embolism			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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 distress			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 29 (0.00%)	1 / 28 (3.57%)	0 / 19 (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
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Cerebrovascular accident			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Dizziness			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	1 / 19 (5.26%)
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 / 29 (0.00%)	0 / 28 (0.00%)	0 / 19 (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
Hemiparesis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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

Syncope			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Presyncope			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 29 (6.90%)	0 / 28 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile bone marrow aplasia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	1 / 19 (5.26%)
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			
Abdominal pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 28 (3.57%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Gastric haemorrhage			

subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	0 / 19 (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 haemorrhage			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Nausea			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	0 / 19 (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
Intestinal obstruction			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Obstruction gastric			
subjects affected / exposed	0 / 29 (0.00%)	1 / 28 (3.57%)	0 / 19 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 29 (0.00%)	1 / 28 (3.57%)	0 / 19 (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
Vomiting			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	0 / 19 (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
Hepatobiliary disorders			
Biliary dilatation			
subjects affected / exposed	0 / 29 (0.00%)	1 / 28 (3.57%)	0 / 19 (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
Cholestasis			

subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Hepatic failure			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Renal failure			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Infections and infestations			
Bacterial sepsis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Urinary tract infection			
subjects affected / exposed	2 / 29 (6.90%)	0 / 28 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Klebsiella sepsis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 29 (10.34%)	0 / 28 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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
Malnutrition			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	0 / 19 (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	Follow-up - Placebo	Follow-up - 30mg/kg BYM338 Late	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	7 / 21 (33.33%)	
number of deaths (all causes)	0	3	
number of deaths resulting from adverse events	0	0	

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	0 / 3 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant neoplasm progression			
subjects affected / exposed	0 / 3 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to central nervous system			
subjects affected / exposed	0 / 3 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angiopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumonia aspiration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ischaemic stroke			
subjects affected / exposed	0 / 3 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile bone marrow aplasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction gastric			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	1 / 3 (33.33%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary dilatation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacterial sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Klebsiella infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			

subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Core - 30 mg/kg BYM338	Core - Placebo	Follow-up - 30 mg/kg BYM338
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 29 (65.52%)	19 / 28 (67.86%)	12 / 19 (63.16%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	3 / 29 (10.34%)	0 / 28 (0.00%)	0 / 19 (0.00%)
occurrences (all)	3	0	0
Hot flush			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	3 / 29 (10.34%)	3 / 28 (10.71%)	1 / 19 (5.26%)
occurrences (all)	3	7	1
Fatigue			
subjects affected / exposed	6 / 29 (20.69%)	3 / 28 (10.71%)	4 / 19 (21.05%)
occurrences (all)	6	4	4
Asthenia			
subjects affected / exposed	2 / 29 (6.90%)	0 / 28 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	1
Pyrexia			
subjects affected / exposed	1 / 29 (3.45%)	2 / 28 (7.14%)	0 / 19 (0.00%)
occurrences (all)	1	2	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Haemoptysis			
subjects affected / exposed	0 / 29 (0.00%)	2 / 28 (7.14%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Epistaxis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 28 (3.57%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Pleural effusion			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Pneumonia aspiration			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Rales			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 29 (6.90%)	0 / 28 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Investigations			
Amylase increased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Gamma-glutamyltransferase increased			

subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	1 / 28 (3.57%) 1	1 / 19 (5.26%) 1
Liver function test abnormal subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 28 (0.00%) 0	1 / 19 (5.26%) 1
Weight decreased subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 3	0 / 28 (0.00%) 0	2 / 19 (10.53%) 2
Injury, poisoning and procedural complications			
Craniocerebral injury subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 28 (0.00%) 0	1 / 19 (5.26%) 1
Fall subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	0 / 28 (0.00%) 0	1 / 19 (5.26%) 1
Laceration subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 28 (0.00%) 0	1 / 19 (5.26%) 1
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	0 / 28 (0.00%) 0	0 / 19 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	2 / 28 (7.14%) 2	0 / 19 (0.00%) 0
Hepatic encephalopathy subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 28 (0.00%) 0	1 / 19 (5.26%) 1
Myoclonus subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 28 (0.00%) 0	1 / 19 (5.26%) 1
Neuropathy peripheral subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	1 / 28 (3.57%) 2	0 / 19 (0.00%) 0
Tremor			

subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 28 (0.00%) 0	1 / 19 (5.26%) 1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 29 (13.79%)	6 / 28 (21.43%)	2 / 19 (10.53%)
occurrences (all)	4	6	2
Neutropenia			
subjects affected / exposed	3 / 29 (10.34%)	3 / 28 (10.71%)	2 / 19 (10.53%)
occurrences (all)	3	6	2
Leukopenia			
subjects affected / exposed	3 / 29 (10.34%)	1 / 28 (3.57%)	1 / 19 (5.26%)
occurrences (all)	4	2	1
Thrombocytopenia			
subjects affected / exposed	2 / 29 (6.90%)	2 / 28 (7.14%)	1 / 19 (5.26%)
occurrences (all)	2	2	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 29 (6.90%)	3 / 28 (10.71%)	0 / 19 (0.00%)
occurrences (all)	2	3	0
Ascites			
subjects affected / exposed	2 / 29 (6.90%)	1 / 28 (3.57%)	1 / 19 (5.26%)
occurrences (all)	2	1	1
Dysphagia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 28 (3.57%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	5 / 29 (17.24%)	3 / 28 (10.71%)	1 / 19 (5.26%)
occurrences (all)	5	3	1
Constipation			
subjects affected / exposed	2 / 29 (6.90%)	1 / 28 (3.57%)	0 / 19 (0.00%)
occurrences (all)	2	1	0
Nausea			
subjects affected / exposed	5 / 29 (17.24%)	1 / 28 (3.57%)	0 / 19 (0.00%)
occurrences (all)	5	1	0
Stomatitis			

subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	3 / 28 (10.71%) 3	2 / 19 (10.53%) 2
Vomiting subjects affected / exposed occurrences (all)	4 / 29 (13.79%) 4	1 / 28 (3.57%) 1	0 / 19 (0.00%) 0
Hepatobiliary disorders Jaundice subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 28 (0.00%) 0	1 / 19 (5.26%) 1
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	0 / 28 (0.00%) 0	0 / 19 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	2 / 28 (7.14%) 2	0 / 19 (0.00%) 0
Swelling face subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 28 (0.00%) 0	1 / 19 (5.26%) 1
Renal and urinary disorders Urinary incontinence subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 28 (0.00%) 0	1 / 19 (5.26%) 1
Bladder irritation subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 28 (0.00%) 0	1 / 19 (5.26%) 1
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	2 / 28 (7.14%) 2	1 / 19 (5.26%) 1
Flank pain subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 28 (0.00%) 0	1 / 19 (5.26%) 1
Muscle spasms subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	1 / 28 (3.57%) 1	0 / 19 (0.00%) 0

Pain in extremity subjects affected / exposed occurrences (all)	3 / 29 (10.34%) 3	0 / 28 (0.00%) 0	0 / 19 (0.00%) 0
Rhabdomyolysis subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 28 (0.00%) 0	1 / 19 (5.26%) 1
Infections and infestations			
Gingival infection subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 28 (0.00%) 0	1 / 19 (5.26%) 1
Candida infection subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	2 / 28 (7.14%) 2	0 / 19 (0.00%) 0
Herpes zoster subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 28 (0.00%) 0	1 / 19 (5.26%) 1
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 28 (0.00%) 0	2 / 19 (10.53%) 2
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 28 (0.00%) 0	1 / 19 (5.26%) 1
Septic shock subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 28 (0.00%) 0	1 / 19 (5.26%) 1
Wound infection staphylococcal subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 28 (0.00%) 0	1 / 19 (5.26%) 1
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	3 / 29 (10.34%) 3	0 / 28 (0.00%) 0	0 / 19 (0.00%) 0
Dehydration subjects affected / exposed occurrences (all)	4 / 29 (13.79%) 4	1 / 28 (3.57%) 2	0 / 19 (0.00%) 0
Hypoalbuminaemia			

subjects affected / exposed	2 / 29 (6.90%)	1 / 28 (3.57%)	0 / 19 (0.00%)
occurrences (all)	2	1	0
Hypokalaemia			
subjects affected / exposed	2 / 29 (6.90%)	2 / 28 (7.14%)	0 / 19 (0.00%)
occurrences (all)	2	2	0
Hypocalcaemia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Hypomagnesaemia			
subjects affected / exposed	2 / 29 (6.90%)	1 / 28 (3.57%)	0 / 19 (0.00%)
occurrences (all)	2	1	0
Hyponatraemia			
subjects affected / exposed	3 / 29 (10.34%)	1 / 28 (3.57%)	0 / 19 (0.00%)
occurrences (all)	3	1	0
Lactic acidosis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Malnutrition			
subjects affected / exposed	2 / 29 (6.90%)	1 / 28 (3.57%)	1 / 19 (5.26%)
occurrences (all)	2	1	1

Non-serious adverse events	Follow-up - Placebo	Follow-up - 30mg/kg BYM338 Late	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	13 / 21 (61.90%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	2 / 21 (9.52%)	
occurrences (all)	0	2	
General disorders and administration site conditions			

Oedema peripheral subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 21 (4.76%) 1	
Fatigue subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 21 (4.76%) 1	
Asthenia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 21 (0.00%) 0	
Pyrexia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 21 (4.76%) 2	
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 21 (0.00%) 0	
Nasal congestion subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 21 (0.00%) 0	
Haemoptysis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 21 (0.00%) 0	
Epistaxis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 21 (0.00%) 0	
Pleural effusion subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 21 (4.76%) 1	
Pneumonia aspiration subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 21 (0.00%) 0	
Rales subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 21 (0.00%) 0	
Wheezing			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 21 (0.00%) 0	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 21 (0.00%) 0	
Investigations Amylase increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 21 (9.52%) 2	
Blood bilirubin increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 21 (0.00%) 0	
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 21 (4.76%) 1	
Liver function test abnormal subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 21 (0.00%) 0	
Weight decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 21 (0.00%) 0	
Injury, poisoning and procedural complications Craniocerebral injury subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 21 (0.00%) 0	
Fall subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 21 (0.00%) 0	
Laceration subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 21 (0.00%) 0	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 21 (4.76%) 1	

Headache			
subjects affected / exposed	0 / 3 (0.00%)	2 / 21 (9.52%)	
occurrences (all)	0	2	
Hepatic encephalopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Myoclonus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Neuropathy peripheral			
subjects affected / exposed	0 / 3 (0.00%)	2 / 21 (9.52%)	
occurrences (all)	0	3	
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	3 / 21 (14.29%)	
occurrences (all)	1	4	
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	3	
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	2	
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Ascites			
subjects affected / exposed	1 / 3 (33.33%)	1 / 21 (4.76%)	
occurrences (all)	1	1	
Dysphagia			

subjects affected / exposed	1 / 3 (33.33%)	1 / 21 (4.76%)	
occurrences (all)	1	1	
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	5 / 21 (23.81%)	
occurrences (all)	0	7	
Constipation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 21 (0.00%)	
occurrences (all)	3	0	
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	2 / 21 (9.52%)	
occurrences (all)	0	2	
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	2 / 21 (9.52%)	
occurrences (all)	0	3	
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 3 (33.33%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	0 / 3 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Swelling face			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Bladder irritation			

subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Rhabdomyolysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Gingival infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Candida infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Herpes zoster			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Septic shock			

subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Wound infection staphylococcal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Lactic acidosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Malnutrition			
subjects affected / exposed	0 / 3 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 June 2011	Amendment 1 : Revision of Study Design: The study will consist of a Core period, an Open Label Follow-up period, and a Vital Status follow-up period. The Core period will be unchanged with a single dose of BYM338 or placebo at Visit 3. Total duration of the Core period will be 8 weeks. The open-label Extension period will be removed. An eight week open-label treatment/Follow up period will be added: At Visit 8, week 11 a single dose of BYM338 will be offered to all patients who received placebo at Visit 3. Patients who received active drug at Visit 3 will be followed for an additional 8 weeks (total of 16 weeks), but will NOT receive any additional doses of BYM338. Revision of the following Inclusion #3 & 4 and Exclusion #2, 3, 4, 6 Criteria Inclusion #3: Eliminate requirement for 4 weeks of stable 2nd line chemotherapy for pancreatic cancer. Patients must be tolerating chemotherapy with respect to nausea/vomiting and dietary intake before starting study drug, without specifying a time frame. Inclusion #4: Define "simple starvation." Add a provision to include: In patients with 2+ or greater pitting edema of the legs, documented weight loss > 2% over 4 weeks, not due to diuretic therapy, is acceptable for inclusion. Exclusion #2: Clarify radiation that is excluded for 4 weeks refers only to radiation of the soft tissues of the chest, abdomen, or brain. Exclusion #3: Add "uncontrolled pain" after steatorrhea. Exclusion #4: Add "uncontrolled" in front of exocrine pancreas dysfunction. Exclusion #6: Delete including major depression. Delete Food Frequency Questionnaire (FFQ) and food diary; replace with 2-day Food Record. Delete requirement of MRI of primary tumor. CT will be allowed for primary tumor progression imaging. MRI will remain the method used for measuring TMV. Add: Tumor progression will be followed using RECIST criteria. Safety labs (hematology, coagulations, chemistry) will be measured by local laboratories,
25 July 2011	Amendment 2 : The protocol is being amended to address comments from a Health Authority in addition to updating the text for a serious adverse event, provide clarifications and correct minor issues. Revision of Serious Adverse Event text: The text in amendment 1 stated the SAE occurred 4 weeks after dosing. The text has been updated after the investigator updated the SAE report. The Human Pharmacokinetic data was updated to reflect data from a recent Pharmacokinetic analysis. Inclusion of "maintenance therapy" was added to inclusion criteria #3. At some centers, patients are maintained on a chemotherapeutic regimen if they demonstrate partial response or stable disease; to allow such patients to participate in this study, we are amending the protocol to include this approach as "maintenance (chemo) therapy". Inclusion criteria #5, "unintentional" added before weight loss Visit window for week 8 post dose is +/- 7 days to allow for more flexibility.
06 December 2011	Amendment 3: The purpose of this amendment is to: 1. Incorporate additional monitoring measures based on Adverse events observed with a compound with a related mechanism of action (supine and standing blood pressure and more specific physical examination) 2. Extend the timeframe for required use of highly effective contraception for women of child-bearing potential to 14 weeks from the previously mandated 8 weeks after stopping treatment, based on a new half-life calculation 3. Correct minor inconsistencies in the document and update information, i.e. serious adverse event information updated.

07 March 2012	Amendment 4: The purpose of this amendment is to: To provide clarity on inclusion criteria for lines of chemotherapy for NSCLC and pancreatic patients, based on feedback from active investigators. Available chemotherapeutic agents have been used in different combination and in varying orders depending on the judgement of treating oncologist and tumor response. As a result of longer survival of cancer patients there is a need for a more prolonged and aggressive use of chemtherapeutic agents occasionally known as 3rd or 4th line of therapy In addition, cancer cachexia has been usually manifested in advanced cases with 3rd or 4th line of therapies. In order to capture the appropriate population for this study with the proper weight loss and expected survival, related inclusion criteria have been revised. Correct the timeframe for capturing Serious Adverse Events (SAE's) from 60 days post dose to 30 days post End of Study (EOS) visit. Remove the blood draw for pharmacogenomics at screening. Clarify windows for the study visits to allow for increased flexibility for the sites. Correct inconsistencies in the document and update information, i.e. Serious Adverse Event information updated.
25 September 2012	Amendment 5: The primary purpose of this amendment is to introduce an internal Data Monitoring Committee (DMC) separate from the BYM338 project team, which is being implemented in all new and ongoing phase 1 and 2a studies with BYM338. This DMC is being introduced at the request of the US FDA because of the new mode of action of BYM338, for which the safety profile is not fully characterized, and because of safety concerns observed by FDA with a non-Novartis molecule with a similar mode of action.
30 July 2013	Amendment 6: The purpose of this amendment is to address the administrative inconsistencies and to allow for additional interim analyses for decision-making purposes if needed.
10 March 2014	Amendment 7: In the original protocol, the review of previous concomitant medications was limited to 8 weeks prior to the start of the study. However, it has been recognized that knowledge of concomitant medication administration (e.g., chemotherapy) given > 8 weeks prior to study start provides a fuller context from which to interpret responses to treatment in this study. Therefore the protocol is being amended to allow for collection of information on concomitant medications from the time of diagnosis of the current disease stage.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported