Clinical trial results:
Open Label, Adaptive Design, Ascending, Multiple-Dose Study to Evaluate Safety and Efficacy of BMS-986004 in Adult Subjects with Primary Immune Thrombocytopenia (ITP)

Summary

EudraCT number	2014-001429-33
Trial protocol	GB PL
Global end of trial date	22 January 2018

Results information

Result version number	v1 (current)
This version publication date	02 February 2019
First version publication date	02 February 2019

Trial information

Trial identification

Sponsor protocol code	IM140-103

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium,
Public contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	22 January 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to assess the overall safety and tolerability of multiple doses of BMS-986004, when administered in subjects with chronic ITP.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 November 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: 4
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Georgia: 4
Country: Number of subjects enrolled	Moldova, Republic of: 3
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 5
Worldwide total number of subjects	26
EEA total number of subjects	8

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)	21
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

46 subjects were enrolled in the study and 26 subjects entered the treatment period. Of the 20 who did not enter the treatment period, 19 did not meet study criteria and 1 experienced an adverse event.

Period 1

Period 1 title	Short Term Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	BMS 75mg

Arm description:

BMS-986004 dose level 75 mg

Arm type	Experimental
Investigational medicinal product name	BMS-986004
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

75 mg intravenous

Arm title	BMS 225mg

Arm description:

BMS-986004 dose level 225 mg

Arm type	Experimental
Investigational medicinal product name	BMS-986004
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

225 mg intravenous

Arm title	BMS 675 mg

Arm description:

BMS-986004 dose level 675 mg

Arm type	Experimental
Investigational medicinal product name	BMS-986004
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

675 mg intravenous

Arm title	BMS 1500 mg
Arm description: BMS-986004 dose level 1500 mg	
Arm type	Experimental
Investigational medicinal product name	BMS-986004
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use
Dosage and administration details: 1500 mg intravenous	

Number of subjects in period 1	BMS 75mg	BMS 225mg	BMS 675 mg
Started	5	6	5
Completed	0	0	1
Not completed	5	6	4
ST complete, not entering LTE	4	6	4
Lost to follow-up	1	-	-
Lack of efficacy	-	-	-

Number of subjects in period 1	BMS 1500 mg
Started	10
Completed	4
Not completed	6
ST complete, not entering LTE	5
Lost to follow-up	-
Lack of efficacy	1

Period 2	
Period 2 title	Long Term Extension
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded
Arms	
Are arms mutually exclusive?	Yes

Arm title	BMS 675 mg
Arm description: BMS-986004 dose level 675 mg	
Arm type	Experimental
Investigational medicinal product name	BMS-986004
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use
Dosage and administration details: 675 mg intravenous	
Arm title	BMS 1500 mg
Arm description: BMS-986004 dose level 1500 mg	
Arm type	Experimental
Investigational medicinal product name	BMS-986004
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use
Dosage and administration details: 1500 mg intravenous	

Number of subjects in period 2	BMS 675 mg	BMS 1500 mg
Started	1	4
Completed	1	3
Not completed	0	1
Adverse event, serious fatal	-	1

Baseline characteristics

Reporting groups	
Reporting group title	BMS 75mg
Reporting group description:	
BMS-986004 dose level 75 mg	
Reporting group title	BMS 225mg
Reporting group description:	
BMS-986004 dose level 225 mg	
Reporting group title	BMS 675 mg
Reporting group description:	
BMS-986004 dose level 675 mg	
Reporting group title	BMS 1500 mg
Reporting group description:	
BMS-986004 dose level 1500 mg	

Reporting group values	BMS 75mg	BMS 225mg	BMS 675 mg
Number of subjects	5	6	5
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)	4	6	5
From 65-84 years	1	0	0
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	52.8	43.2	34.2
standard deviation	± 20.58	± 16.33	± 16.93
Sex: Female, Male			
Units: Subjects			
Female	2	2	4
Male	3	4	1
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	4	5	5
More than one race	0	0	0
Unknown or Not Reported	1	0	0
Ethnicity (NIH/OMB)			

Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	1	4	4
Unknown or Not Reported	4	2	1

Reporting group values	BMS 1500 mg	Total	
Number of subjects	10	26	
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)	6	21	
From 65-84 years	4	5	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	55.3		
standard deviation	± 16.09	-	
Sex: Female, Male Units: Subjects			
Female	4	12	
Male	6	14	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	2	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	1	
White	7	21	
More than one race	0	0	
Unknown or Not Reported	1	2	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	8	17	
Unknown or Not Reported	2	9	

End points

End points reporting groups

Reporting group title	BMS 75mg
Reporting group description: BMS-986004 dose level 75 mg	
Reporting group title	BMS 225mg
Reporting group description: BMS-986004 dose level 225 mg	
Reporting group title	BMS 675 mg
Reporting group description: BMS-986004 dose level 675 mg	
Reporting group title	BMS 1500 mg
Reporting group description: BMS-986004 dose level 1500 mg	
Reporting group title	BMS 675 mg
Reporting group description: BMS-986004 dose level 675 mg	
Reporting group title	BMS 1500 mg
Reporting group description: BMS-986004 dose level 1500 mg	

Primary: Number of subjects with adverse events (AEs) and serious adverse events (SAEs): Short term and Long term

End point title	Number of subjects with adverse events (AEs) and serious adverse events (SAEs): Short term and Long term[1]

End point description:

The primary objective to establish safety was measured by the primary endpoints of AEs and SAEs for both Short term and Long term periods

End point type	Primary

End point timeframe:

Day 1 to Day 141 (Short term) and Day 1 to Day 398 (Long term)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary statistics were planned for this endpoint

End point values	BMS 75mg	BMS 225mg	BMS 675 mg	BMS 1500 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	5	10
Units: Subjects				
Number of subjects with AEs|	1	5	5	9
Number of subjects with SAEs|	0	0	1	1

Statistical analyses

No statistical analyses for this end point

Primary: Number of ECG abnormalities

End point title	Number of ECG abnormalities[2]

End point description:

The primary objective to establish safety was measured by investigator identified Electrocardiogram Abnormalities for both Short term and Long term periods. ECG parameters included heart rate, PR interval, QRS interval, and QTcF interval (QT interval corrected for heart rate)

End point type	Primary

End point timeframe:

Day 1 to Day 141 (Short term) and Day 1 to Day 398 (Long term)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary statistics were planned for this endpoint

End point values	BMS 75mg	BMS 225mg	BMS 675 mg	BMS 1500 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	5	10
Units: Events				
Screening	1	3	2	3
Day 1	1	2	2	3
Day 71	0	2	0	0
Day 72	1	0	1	1
End of Treatment	1	3	2	1
Long term Day 1	0	0	0	2
Long term Day 71	0	0	0	2
End of Long term	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Primary: Number of laboratory abnormalities of Safety biomarkers: d-Dimer and Thrombin anti-Thrombin (TAT)

End point title	Number of laboratory abnormalities of Safety biomarkers: d-Dimer and Thrombin anti-Thrombin (TAT)[3]

End point description:

D-dimer and thrombin antithrombin (TAT) in plasma were quantified as measures of Thromboembolism (TE) risk.

End point type	Primary

End point timeframe:

Day 1 to Day 141 (Short term) and Day 1 to Day 398 (Long Term)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary statistics were planned for this endpoint

End point values	BMS 75mg	BMS 225mg	BMS 675 mg	BMS 1500 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	5	10
Units: Events				
# of events: d-Dimer, Normal	56	81	60	106
# of events: d-Dimer, High	12	14	15	17
# of events: TAT Complex, Normal	52	71	46	112
# of events: TAT Complex, High	21	30	31	28

Statistical analyses

No statistical analyses for this end point

Secondary: Response rate (RR) of BMS-986004: Short term and Long term

End point title	Response rate (RR) of BMS-986004: Short term and Long term

End point description:

RR is defined as the proportion of subjects who are responders

End point type	Secondary

End point timeframe:

Day 1 to Day 141 (Short term) and Day 1 to Day 398 (Long term)

End point values	BMS 75mg	BMS 225mg	BMS 675 mg	BMS 1500 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	5	10
Units: No units				
number (not applicable)				
RR during ST	0.2	0.3	0.4	0.4
RR during LTE (# analyzed = 0, 0, 1, 4)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum observed serum concentration (Cmax) of BMS-986004

End point title	Maximum observed serum concentration (Cmax) of BMS-986004

End point description:

Pharmacokinetic parameter (Cmax) of BMS-986004, derived from serum concentration versus time. Pharmacokinetic Population is defined as all subjects who receive any study medication and have any available concentration-time data. Additionally, the evaluable PK Population is defined as subjects who have adequate PK profiles.

End point type	Secondary

End point timeframe:

Day 1 till Day 141

End point values	BMS 75mg	BMS 225mg	BMS 675 mg	BMS 1500 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	5	10
Units: ng/mL				
arithmetic mean (standard deviation)				
Cmax Day 1| (Subjects analyzed per arm = 2,6,4,9)	19353.5 (± 6131.32)	59478.8 (± 10021.04)	177706.3 (± 37924.30)	296561.9 (± 119530.86)
Cmax Day 71| (Subjects analyzed per arm =0,4,6,13)	9999 (± 9999)	62469.8 (± 27336.64)	186981.0 (± 22216.82)	373588.9 (± 89833.77)

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the concentration-time curve in one dosing interval [AUC(TAU)] of BMS-986004

End point title	Area under the concentration-time curve in one dosing interval [AUC(TAU)] of BMS-986004

End point description:

Pharmacokinetics of BMS-986004 were derived from serum concentration versus time data. AUC(TAU) = Area under the concentration-time curve in one dosing interval. Pharmacokinetic (PK) Population, defined as all subjects who receive any study medication and have any available concentration-time data. Additionally, the evaluable PK Population is defined as subjects who have adequate PK profiles.

End point type	Secondary

End point timeframe:

From Day 1 till Day 141

End point values	BMS 75mg	BMS 225mg	BMS 675 mg	BMS 1500 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	5	10
Units: h*ng/mL				
arithmetic mean (standard deviation)				
AUC(TAU) Day 1| (Subjects per arm = 2,6,4,9)	915500 (± 196460)	3445000 (± 708290)	11440000 (± 3041300)	18370000 (± 7351000)
AUC(TAU) Day 71| (Subjects per arm = 0,4,6,13)	9999 (± 9999)	4408000 (± 3313000)	11460000 (± 2124900)	26500000 (± 9366800)

Statistical analyses

No statistical analyses for this end point

Secondary: Trough observed serum concentration (Ctrough) of BMS-986004

End point title	Trough observed serum concentration (Ctrough) of BMS-986004

End point description:

Pharmacokinetics of BMS-986004 were derived from serum concentration versus time data. Ctrough = Trough observed serum concentration. Pharmacokinetic Population is defined as all subjects who receive any study medication and have any available concentration-time data. Additionally, the evaluable PK Population is defined as subjects who have adequate PK profiles.

End point type	Secondary

End point timeframe:

From Day 1 till Day 141

End point values	BMS 75mg	BMS 225mg	BMS 675 mg	BMS 1500 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	5	10
Units: ng/mL				
arithmetic mean (standard deviation)				
Ctrough, Day 15| (Subjects per arm: 5,6,5,10)	978.0 (± 1080.82)	2373.0 (± 1182.00)	7556.4 (± 1952.53)	15282.5 (± 9710.77)
Ctrough, Day 29| (Subjects per arm:5,6,5,10)	1011.4 (± 999.13)	3157.7 (± 1458.85)	10236.0 (± 3737.42)	21353.6 (± 14144.90)
Ctrough, Day 43|(Subjects per arm: 5,6,5,9)	1207.0 (± 852.88)	3527.7 (± 1576.34)	9416.2 (± 4410.57)	19105.3 (± 14980.50)
Ctrough, Day 57|(Subjects per arm: 0,4,6,14)	9999 (± 9999)	25339.5 (± 49053.16)	3360.5 (± 1082.75)	20553.1 (± 19099.39)
Ctrough, Day 71|(Subjects per arm: 0,4,6,13)	9999 (± 9999)	3466.0 (± 3209.75)	8347.7 (± 3215.32)	25057.3 (± 18007.59)
Ctrough, Day 85|(Subjects per arm:0,4,6,13)	9999 (± 9999)	4018.8 (± 4099.35)	9075.7 (± 4268.76)	24308.9 (± 19213.61)

Statistical analyses

No statistical analyses for this end point

Secondary: Total body clearance (CLT) of BMS-986004

End point title	Total body clearance (CLT) of BMS-986004

End point description:

Pharmacokinetics of BMS-986004 were derived from serum concentration versus time data.Pharmacokinetic Population, defined as all subjects who receive any study medication and have any available concentration-time data. Additionally, the evaluable PK Population is defined as subjects who have adequate PK profiles.

End point type	Secondary

End point timeframe:

From Day 1 till Day 141

End point values	BMS 75mg	BMS 225mg	BMS 675 mg	BMS 1500 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	5	10
Units: L/H				
arithmetic mean (standard deviation)				
CLT Day 1| (Subjects per arm:2,6,4,8)	0.0789 (± 0.01514)	0.0618 (± 0.01617)	0.0561 (± 0.01395)	0.0860 (± 0.03037)
CLT Day 71|(Subjects per arm:0,4,6,13)	9999 (± 9999)	0.0716 (± 0.04106)	0.0611 (± 0.01449)	0.0628 (± 0.02061)

Statistical analyses

No statistical analyses for this end point

Secondary: AUC accumulation index (AI_AUC) of BMS-986004

End point title	AUC accumulation index (AI_AUC) of BMS-986004

End point description:

AUC accumulation index (AI_AUC) = ratio of AUC(TAU) at steady state to AUC(TAU) after the first dose of BMS-986004. Pharmacokinetic Population, defined as all subjects who receive any study medication and have any available concentration-time data. Additionally, the evaluable PK Population is defined as subjects who have adequate PK profiles.

End point type	Secondary

End point timeframe:

Day 1 till Day 141

End point values	BMS 75mg	BMS 225mg	BMS 675 mg	BMS 1500 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	5	10
Units: Tau				
arithmetic mean (standard deviation)				
AI_AUC(TAU) (Subjects per arm: 0,0,0,12)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	1.7996 (± 0.597881)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All non-serious adverse events (NSAEs) and serious adverse events (SAEs) are reported from short-term period (Day 1 to Day 141) and long-term extension period (Day 1 to Day 398).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	BMS-986004 75 mg

Reporting group description:

Subjects with received BMS-986004 75 milligram (mg) as intravenous (IV) solution.

Reporting group title	BMS-986004 675 mg

Reporting group description:

Subjects with primary ITP received BMS-986004 675 mg as IV solution.

Reporting group title	BMS-986004 1500 mg

Reporting group description:

Subjects with primary ITP received BMS-986004 1500 mg as IV solution.

Reporting group title	BMS-986004 225 mg

Reporting group description:

Subjects with primary ITP received BMS-986004 225 mg as IV solution.

Serious adverse events	BMS-986004 75 mg	BMS-986004 675 mg	BMS-986004 1500 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Serious adverse events	BMS-986004 225 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	0 / 6 (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: 5 %

Non-serious adverse events	BMS-986004 75 mg	BMS-986004 675 mg	BMS-986004 1500 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	5 / 5 (100.00%)	9 / 10 (90.00%)
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Peripheral coldness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	4 / 10 (40.00%)
occurrences (all)	0	0	4
Feeling cold			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Injection site reaction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			

Allergy to animal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Social circumstances			
Exercise lack of			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	3	0
Cough			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Pharyngeal haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Neurosis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Stress			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Heart sounds abnormal			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Platelet count decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Platelet count increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Weight decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Dizziness			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Haemorrhage intracranial			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Migraine			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 5 (40.00%)	1 / 10 (10.00%)
occurrences (all)	0	2	1

Iron deficiency anaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Microcytic anaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Faeces discoloured			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Petechiae			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Purpura			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	2 / 10 (20.00%)
occurrences (all)	0	1	2
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Arthritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Osteoporosis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gingival bleeding			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Phlebitis infective			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hypokalaemia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hypophosphataemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Non-serious adverse events	BMS-986004 225 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)		
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Peripheral coldness			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Feeling cold			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection site reaction			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Peripheral swelling			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Allergy to animal			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Social circumstances			
Exercise lack of			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pharyngeal haemorrhage			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Productive cough			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Psychiatric disorders			
Neurosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Stress			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Heart sounds abnormal			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Platelet count decreased			

subjects affected / exposed occurrences (all) Platelet count increased subjects affected / exposed occurrences (all) Weight decreased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0		
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Haemorrhage intracranial subjects affected / exposed occurrences (all) Migraine subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Iron deficiency anaemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1 0 / 6 (0.00%) 0		

Microcytic anaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Abdominal pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Faeces discoloured subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Haemorrhoidal haemorrhage subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Mouth haemorrhage subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Mouth ulceration subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Nausea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Stomatitis subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Skin and subcutaneous tissue disorders Dermatitis contact subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Petechiae subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Purpura			

subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0		
Renal and urinary disorders Micturition urgency subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0		
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Arthritis subjects affected / exposed occurrences (all) Muscular weakness subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Musculoskeletal pain subjects affected / exposed occurrences (all) Osteoporosis subjects affected / exposed occurrences (all) Gingival bleeding subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1		
Infections and infestations			

Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Lower respiratory tract infection			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Periodontitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Phlebitis infective			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Respiratory tract infection viral			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 August 2016	The purpose of this amendment is to add Long Term Extension (LTE) period to the study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported