Clinical trial results:
A Phase 2, Open-label, Randomized Study to Evaluate Safety and Efficacy of Momelotinib in Subjects with Polycythemia Vera or Essential Thrombocythemia

Summary

EudraCT number	2013-004105-11
Trial protocol	DE
Global end of trial date	07 May 2015

Results information

Result version number	v1 (current)
This version publication date	22 May 2016
First version publication date	22 May 2016

Trial information

Trial identification

Sponsor protocol code	GS-US-354-0101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01998828
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Clinical Trial Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.com
Scientific contact	Clinical Trial Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.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	07 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 March 2015
Global end of trial reached?	Yes
Global end of trial date	07 May 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This open-label study was to determine the safety and efficacy of momelotinib in participants with either polycythemia vera (PV) or essential thrombocythemia (ET) who had not yet received treatment with a Janus kinase (JAK) inhibitor.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 February 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	United States: 21
Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	Canada: 3
Worldwide total number of subjects	39
EEA total number of subjects	9

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)	27
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Europe, North America, and Australia. The first participant was screened on 19 February 2014. The last study visit occurred on 07 May 2015.

Pre-assignment

Screening details:

48 participants were screened.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	MMB 100 mg (PV Cohort)

Arm description:

Participants with polycythemia vera received MMB 100 mg for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Momelotinib
Investigational medicinal product code	
Other name	GS-0387
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Momelotinib (MMB) 100 mg, 150 mg, or 200 mg once daily

Arm title	MMB 200 mg (PV Cohort)

Arm description:

Participants with polycythemia vera received MMB 200 mg for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Momelotinib
Investigational medicinal product code	
Other name	GS-0387
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Momelotinib (MMB) 100 mg, 150 mg, or 200 mg once daily

Arm title	MMB 100 mg (ET Cohort)

Arm description:

Participants with essential thrombocythemia received MMB 100 mg for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Momelotinib
Investigational medicinal product code	
Other name	GS-0387
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
Momelotinib (MMB) 100 mg, 150 mg, or 200 mg once daily

Arm title	MMB 200 mg (ET Cohort)
Arm description: Participants with essential thrombocythemia received MMB 200 mg for 24 weeks.	
Arm type	Experimental
Investigational medicinal product name	Momelotinib
Investigational medicinal product code	
Other name	GS-0387
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
Momelotinib (MMB) 100 mg, 150 mg, or 200 mg once daily

Number of subjects in period 1	MMB 100 mg (PV Cohort)	MMB 200 mg (PV Cohort)	MMB 100 mg (ET Cohort)
Started	14	14	5
Completed	5	5	3
Not completed	9	9	2
Subject Withdrew Consent	2	1	-
Adverse event, non-fatal	3	4	-
Study Discontinued by Sponsor	2	3	1
Investigator's Discretion	-	1	1
Lost to follow-up	1	-	-
Disease Progression	1	-	-

Number of subjects in period 1	MMB 200 mg (ET Cohort)
Started	6
Completed	2
Not completed	4
Subject Withdrew Consent	1
Adverse event, non-fatal	1
Study Discontinued by Sponsor	1
Investigator's Discretion	1
Lost to follow-up	-
Disease Progression	-

Baseline characteristics

Reporting groups	
Reporting group title	MMB 100 mg (PV Cohort)
Reporting group description:	
Participants with polycythemia vera received MMB 100 mg for 24 weeks.	
Reporting group title	MMB 200 mg (PV Cohort)
Reporting group description:	
Participants with polycythemia vera received MMB 200 mg for 24 weeks.	
Reporting group title	MMB 100 mg (ET Cohort)
Reporting group description:	
Participants with essential thrombocythemia received MMB 100 mg for 24 weeks.	
Reporting group title	MMB 200 mg (ET Cohort)
Reporting group description:	
Participants with essential thrombocythemia received MMB 200 mg for 24 weeks.	

Reporting group values	MMB 100 mg (PV Cohort)	MMB 200 mg (PV Cohort)	MMB 100 mg (ET Cohort)
Number of subjects	14	14	5
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 58.7 ± 16.8	 61.3 ± 6.54	 60.8 ± 15.78
Gender categorical Units: Subjects			
Female	7	4	3
Male	7	10	2

Reporting group values	MMB 200 mg (ET Cohort)	Total	
Number of subjects	6	39	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 52 ± 11.93	 -	
Gender categorical Units: Subjects			
Female	2	16	
Male	4	23	

End points

End points reporting groups

Reporting group title	MMB 100 mg (PV Cohort)
Reporting group description:	
Participants with polycythemia vera received MMB 100 mg for 24 weeks.	
Reporting group title	MMB 200 mg (PV Cohort)
Reporting group description:	
Participants with polycythemia vera received MMB 200 mg for 24 weeks.	
Reporting group title	MMB 100 mg (ET Cohort)
Reporting group description:	
Participants with essential thrombocythemia received MMB 100 mg for 24 weeks.	
Reporting group title	MMB 200 mg (ET Cohort)
Reporting group description:	
Participants with essential thrombocythemia received MMB 200 mg for 24 weeks.	

Primary: Overall response rate

End point title	Overall response rate[1]
End point description:	
Intent-to-Treat Analysis Set: all participants who are randomized regardless of whether they receive any MMB.	
End point type	Primary
End point timeframe:	
Up to 24 weeks	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned or performed.

End point values	MMB 100 mg (PV Cohort)	MMB 200 mg (PV Cohort)	MMB 100 mg (ET Cohort)	MMB 200 mg (ET Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	14	5	6
Units: percentage of participants				
number (confidence interval 90%)	0 (0 to 19.3)	14.3 (2.6 to 38.5)	0 (0 to 45.1)	0 (0 to 39.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Confirmed overall response rate

End point title	Confirmed overall response rate
End point description:	
Intent-to-Treat Analysis Set	
End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	MMB 100 mg (PV Cohort)	MMB 200 mg (PV Cohort)	MMB 100 mg (ET Cohort)	MMB 200 mg (ET Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	14	5	6
Units: percentage of participants				
number (confidence interval 90%)	0 (0 to 19.3)	7.1 (0.4 to 29.7)	0 (0 to 45.1)	0 (0 to 39.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with hematocrit < 45% in the absence of phlebotomy that lasts at least 4 weeks

End point title	Percentage of participants with hematocrit < 45% in the absence of phlebotomy that lasts at least 4 weeks[2]

End point description:

Participants in the Intent-to-Treat Analysis Set from the PV Cohort were analyzed.

End point type	Secondary

End point timeframe:

Up to 24 weeks

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Hematocrit response was only evaluated in the PV Cohort.

End point values	MMB 100 mg (PV Cohort)	MMB 200 mg (PV Cohort)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: percentage of participants				
number (confidence interval 90%)	28.6 (10.4 to 54)	21.4 (6.1 to 46.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with WBC < 10 x 10^9/L that lasts at least 4 weeks

End point title	Percentage of participants with WBC < 10 x 10^9/L that lasts at least 4 weeks

End point description: Intent-to-Treat Analysis Set	
End point type	Secondary
End point timeframe: Up to 24 weeks	

End point values	MMB 100 mg (PV Cohort)	MMB 200 mg (PV Cohort)	MMB 100 mg (ET Cohort)	MMB 200 mg (ET Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	14	5	6
Units: percentage of participants				
number (confidence interval 90%)	7.1 (0.4 to 29.7)	35.7 (15.3 to 61)	100 (54.9 to 100)	83.3 (41.8 to 99.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with resolution of palpable splenomegaly that lasts at least 4 weeks

End point title	Percentage of participants with resolution of palpable splenomegaly that lasts at least 4 weeks
End point description: Participants in the Intent-to-Treat Analysis Set with baseline spleen size ≥ 5 cm were evaluated for spleen response and serve as the denominator for the spleen response rate calculation.	
End point type	Secondary
End point timeframe: Up to 24 weeks	

End point values	MMB 100 mg (PV Cohort)	MMB 200 mg (PV Cohort)	MMB 100 mg (ET Cohort)	MMB 200 mg (ET Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	0[3]	0[4]
Units: percentage of participants				
number (confidence interval 90%)	25 (1.3 to 75.1)	33.3 (1.7 to 86.5)	(to)	(to)

Notes:

[3] - No participants in this group had a baseline spleen size ≥ 5 cm.

[4] - No participants in this group had a baseline spleen size ≥ 5 cm.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with ≥ 10 point decrease in modified Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score

(MPNSAF TSS) compared to baseline that lasts at least 12 weeks

End point title	Percentage of participants with ≥ 10 point decrease in modified Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score (MPNSAF TSS) compared to baseline that lasts at least 12 weeks

End point description:

Intent-to-Treat Analysis Set

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	MMB 100 mg (PV Cohort)	MMB 200 mg (PV Cohort)	MMB 100 mg (ET Cohort)	MMB 200 mg (ET Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	14	5	6
Units: percentage of participants				
number (not applicable)	0	7.1	0	16.7

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline through end of study drug treatment (mean exposure: MMB 100 mg PV = 109.0 days; MMB 200 mg PV = 122.1 days; MMB 100 mg ET = 154.4 days; MMB 200 mg ET = 127.2 days) plus 30 days	
Adverse event reporting additional description:	
Safety Analysis Set: all participants in the ITT Analysis Set who received ≥ 1 dose of MMB, with study treatment assignments designated according to the actual treatment received.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups	
Reporting group title	MMB 100 mg (PV Cohort)
Reporting group description:	
Participants with polycythemia vera received MMB 100 mg for 24 weeks.	
Reporting group title	MMB 200 mg (PV Cohort)
Reporting group description:	
Participants with polycythemia vera received MMB 200 mg for 24 weeks.	
Reporting group title	MMB 100 mg (ET Cohort)
Reporting group description:	
Participants with essential thrombocythemia received MMB 100 mg for 24 weeks.	
Reporting group title	MMB 200 mg (ET Cohort)
Reporting group description:	
Participants with essential thrombocythemia received MMB 200 mg for 24 weeks.	

Serious adverse events	MMB 100 mg (PV Cohort)	MMB 200 mg (PV Cohort)	MMB 100 mg (ET Cohort)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	0 / 5 (0.00%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Urinary bladder polyp			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (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

Serious adverse events	MMB 200 mg (ET Cohort)		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary bladder polyp			
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	MMB 100 mg (PV Cohort)	MMB 200 mg (PV Cohort)	MMB 100 mg (ET Cohort)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 14 (85.71%)	14 / 14 (100.00%)	5 / 5 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Myelofibrosis			

subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Skin cancer			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 14 (21.43%)	4 / 14 (28.57%)	0 / 5 (0.00%)
occurrences (all)	3	4	0
Flushing			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Haematoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 14 (14.29%)	4 / 14 (28.57%)	0 / 5 (0.00%)
occurrences (all)	2	4	0
Asthenia			
subjects affected / exposed	1 / 14 (7.14%)	2 / 14 (14.29%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Pyrexia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 14 (0.00%)	1 / 5 (20.00%)
occurrences (all)	2	0	1
Chest pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			

subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Ulcer			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 14 (14.29%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Cough			
subjects affected / exposed	2 / 14 (14.29%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	3	0	0
Asthma			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	2 / 14 (14.29%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Haemoptysis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Productive cough			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Psychiatric disorders			

Depression			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood phosphorus increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Blood uric acid increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Creatinine renal clearance decreased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Platelet count increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Weight increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hand fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			

Palpitations			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 14 (35.71%)	4 / 14 (28.57%)	1 / 5 (20.00%)
occurrences (all)	5	4	2
Dizziness			
subjects affected / exposed	0 / 14 (0.00%)	6 / 14 (42.86%)	0 / 5 (0.00%)
occurrences (all)	0	6	0
Somnolence			
subjects affected / exposed	4 / 14 (28.57%)	2 / 14 (14.29%)	0 / 5 (0.00%)
occurrences (all)	6	2	0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	1 / 5 (20.00%)
occurrences (all)	2	1	1
Paraesthesia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Aura			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Burning sensation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dysaesthesia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Psychomotor hyperactivity			

subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Thrombocytosis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	1 / 5 (20.00%)
occurrences (all)	1	1	1
Iron deficiency anaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Cataract subcapsular			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Ocular discomfort			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 14 (14.29%)	4 / 14 (28.57%)	0 / 5 (0.00%)
occurrences (all)	2	4	0
Diarrhoea			
subjects affected / exposed	2 / 14 (14.29%)	2 / 14 (14.29%)	1 / 5 (20.00%)
occurrences (all)	3	2	3
Vomiting			

subjects affected / exposed	1 / 14 (7.14%)	3 / 14 (21.43%)	0 / 5 (0.00%)
occurrences (all)	1	3	0
Abdominal pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Constipation			
subjects affected / exposed	2 / 14 (14.29%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Flatulence			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Gingival recession			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Salivary hypersecretion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 14 (14.29%)	3 / 14 (21.43%)	0 / 5 (0.00%)
occurrences (all)	3	4	0
Alopecia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0

Night sweats			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Rash			
subjects affected / exposed	0 / 14 (0.00%)	2 / 14 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Cold sweat			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Erythrosis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Skin exfoliation			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 14 (7.14%)	2 / 14 (14.29%)	1 / 5 (20.00%)
occurrences (all)	1	2	1
Bone pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Arthralgia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	1	1	0

Back pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Bronchitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Cellulitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis viral			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Laryngitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			

subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	0 / 5 (0.00%)
occurrences (all)	1	1	0

Non-serious adverse events	MMB 200 mg (ET Cohort)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Myelofibrosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin cancer			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Flushing			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Haematoma			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Oedema			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pain			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ulcer			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Asthma			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Haemoptysis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Insomnia			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Investigations			
Blood phosphorus increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood uric acid increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Creatinine renal clearance decreased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Platelet count increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hand fracture			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Skin abrasion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nervous system disorders			

Headache				
subjects affected / exposed	3 / 6 (50.00%)			
occurrences (all)	4			
Dizziness				
subjects affected / exposed	3 / 6 (50.00%)			
occurrences (all)	3			
Somnolence				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Peripheral sensory neuropathy				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Paraesthesia				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Aura				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Burning sensation				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Disturbance in attention				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Dysaesthesia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Dysgeusia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Psychomotor hyperactivity				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Sciatica				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			

Syncope			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Tremor			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Thrombocytosis			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	3		
Iron deficiency anaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Eye disorders			
Cataract subcapsular			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ocular discomfort			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	3		
Abdominal pain			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Constipation			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gingival recession			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Salivary hypersecretion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Alopecia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Night sweats			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Cold sweat			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Erythrosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin exfoliation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Bone pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Myalgia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cystitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastroenteritis viral			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Laryngitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Sinusitis			

subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Tooth abscess subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Tooth infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 2		
Viral infection subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Vulvovaginal mycotic infection subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Metabolism and nutrition disorders Decreased appetite 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
03 January 2014	Incorporated newly available data and updates to study procedures.
14 July 2014	Updates to study procedures and restrictions based on newly available data.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
22 September 2014	The study was discontinued due to limited efficacy observed in planned interim analyses.	-

Notes:

Limitations and caveats

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

These data represent fewer than the planned number of subjects with limited treatment duration.

Notes: