Clinical trial results:
A PHASE IV, OPEN-LABEL, MULTICENTER STUDY OF DASATINIB IN CHRONIC-PHASE CHRONIC MYELOID LEUKEMIA (CP-CML) PATIENTS WITH CHRONIC LOW-GRADE NONHEMATOLOGIC TOXICITY TO IMATINIB

Summary

EudraCT number	2011-006180-21
Trial protocol	IT DE
Global end of trial date	01 October 2015

Results information

Result version number	v1 (current)
This version publication date	14 October 2016
First version publication date	14 October 2016

Trial information

Trial identification

Sponsor protocol code	CA180-400

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01660906
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chausée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb International Corporation, clinical.trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb International Corporation, 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	01 October 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the frequency of reduction in grade (Grade 2 to 1) or resolution of imatinib-related chronic Grade 1 or Grade 2 non-hematologic adverse events (AEs) within 3 months after switch to dasatinib in subjects with Chronic-Phase Chronic Myeloid Leukemia (CP-CML).

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:

Adults subjects diagnosed with CP-CML that had achieved an optimal response to imatinib (≤ 400 mg/day treatment) who had Grade 1 or 2 non-hematologic AEs persisting for at least 2 months, or recurring at least 3 times in the preceding 12 months, despite best supportive care.

Evidence for comparator: -

Actual start date of recruitment	31 October 2012
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	France: 4
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Korea, Republic of: 22
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	39
EEA total number of subjects	14

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:

The study was conducted at 22 sites in France, Germany, Italy, Republic of Korea, and the United States.

Pre-assignment

Screening details:

A total of 39 subjects were enrolled and treated.

Period 1

Period 1 title	Dasatinib (100 mg) (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Dasatinib (100 mg)

Arm description:

Subjects that were previously on an imatinib therapy were treated with a 100 mg tablet of dasatinib taken orally once a day for up to 12 months while on study.

Arm type	Experimental
Investigational medicinal product name	Dasatinib
Investigational medicinal product code	BMS-354825
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered with dasatinib 100 mg tablet orally once daily for up to 12 months while on study.

Number of subjects in period 1	Dasatinib (100 mg)
Started	39
Completed	36
Not completed	3
Discontinued due to study drug toxicity	3

Baseline characteristics

Reporting groups	
Reporting group title	Dasatinib (100 mg)
Reporting group description:	
Subjects that were previously on an imatinib therapy were treated with a 100 mg tablet of dasatinib taken orally once a day for up to 12 months while on study.	

Reporting group values	Dasatinib (100 mg)	Total	
Number of subjects	39	39	
Age categorical Units: Subjects			
Adults (18-64 years)	27	27	
From 65-84 years	12	12	
Age continuous Units: years			
arithmetic mean	55.1		
standard deviation	± 15.13	-	
Gender categorical Units: Subjects			
Female	18	18	
Male	21	21	
Race/Ethnicity Units: Subjects			
White	12	12	
Black or African American	1	1	
American Indian or Alaska Native	0	0	
Asian	22	22	
Native Hawaiian or Other Pacific Islander	0	0	
Other	4	4	
Imatinib dose at baseline Units: Subjects			
< 400 milligrams	19	19	
400 milligrams	20	20	
Best baseline response			
MR4.5, 4.5- log reduction in gene breakpoint cluster region -abelson murine leukemia viral oncogene (BCR-ABL) transcript from the standardized baseline (0.0032% IS); Major Molecular Response (MMR). Complete cytogenetic response (CCyR). Partial cytogenetic response (PCyR).			
Units: Subjects			
MR4.5	10	10	
MMR	20	20	
CCyR	4	4	
PCyR	2	2	
Cytogenetic Test Not Performed	3	3	
Median time since CML-CP diagnosis			
CML-CP			
Units: months			
median	51.3		
full range (min-max)	3.9 to 214.6	-	

Median duration of imatinib Units: months median full range (min-max)	 51.2 3.1 to 160.4	 -	

End points

End points reporting groups

Reporting group title	Dasatinib (100 mg)

Reporting group description:

Subjects that were previously on an imatinib therapy were treated with a 100 mg tablet of dasatinib taken orally once a day for up to 12 months while on study.

Primary: Number of Imatinib-related Adverse Events (AEs) That Were Resolved, Improved, Remained Unchanged, or Worsened After 3 Months of Dasatinib Treatment

End point title	Number of Imatinib-related Adverse Events (AEs) That Were Resolved, Improved, Remained Unchanged, or Worsened After 3 Months of Dasatinib Treatment[1]

End point description:

Prior to dasatinib treatment, subjects were on imatinib therapy and reported 121 imatinib-related Grade 1 or 2 (Grade1/2) AEs. Dasatinib treatment was administered and its impact on the imatinib-related Grade 1/2 AEs was assessed. Imatinib-related chronic AEs were defined as Grade 1 or 2 non-hematologic AEs persisting for at least 2 months or recurring at least 3 times in the preceding 12 months, despite best supportive care. The severity of an adverse event is ranked based on grades that range from 1 to 4 according to National Cancer Institute - Common Terminology Criteria for Adverse Events (NCI-CTCAE) v4.03. Grade 1=Mild, Grade 2=Moderate, Grade 3=Severe, Grade 4= Potentially Life-threatening or disabling. Resolved, AE no longer present or resolution of imatinib-related chronic Grade 1 or Grade 2 non-hematologic AEs. Improved, AE grade reduced from Grade 2 to Grade 1. Unchanged, AE did not improve or worsen or no change in grade. Worsened, grade increased. All treated subjects.

End point type	Primary

End point timeframe:

From screening up to 3 months after switch to dasatinib

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 descriptive statistics was planned for this safety end-point.

End point values	Dasatinib (100 mg)			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: Number of events				
Resolved	91			
Improved	2			
Unchanged	27			
Worsened	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Subject Reported CML Symptom Severity and Interference by MD Anderson Symptom Inventory (MDASI) CML Score After Switching to Dasatinib

End point title	Change From Baseline in Subject Reported CML Symptom Severity and Interference by MD Anderson Symptom Inventory (MDASI) CML Score After Switching to Dasatinib

End point description:

The MDASI-CML is a validated questionnaire completed by study subjects to assess symptom severity and symptom interference on daily function. These categories are divided into 5 domain summary scores: Core Symptom Severity Score, Interference Score, Symptom Severity Score, CML-Specific Symptom Severity Score, and 5 Most Severe Symptom Score. Scores were evaluated at baseline and after switching to dasatinib on a range from 1 to 10; 1=not present/did not interfere, 10=as bad as you can imagine/interfered completely. All treated subjects. Small "n" refers to the total number of subjects that responded to the survey at the specified interval.

End point type	Secondary

End point timeframe:

Baseline, Month 3, 6, and 12

End point values	Dasatinib (100 mg)			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: Score on a scale				
arithmetic mean (standard deviation)				
Core Symptom Severity Score, Month 3; n=37	-1.35 (± 1.78)			
Core Symptom Severity Score, Month 6; n=36	-1.44 (± 1.84)			
Core Symptom Severity Score, Month 12; n=37	-1.06 (± 1.87)			
Interference Score, Month 3; n=37	-1.24 (± 2.36)			
Interference Score, Month 6; n=35	-1.28 (± 2.45)			
Interference Score, Month 12; n=36	-1.3 (± 2.56)			
Symptom Severity Score, Month 3; n=37	-1.73 (± 1.8)			
Symptom Severity Score, Month 6; n=36	-1.8 (± 1.85)			
Symptom Severity Score, Month 12; n=37	-1.46 (± 1.75)			
CML-specific Symptom Severity Score, Month 3; n=37	-2.52 (± 2.35)			
CML-specific Symptom Severity Score, Month 6; n=36	-2.6 (± 2.15)			
CML-specific Symptom Severity Score,Month 12; n=36	-2.24 (± 1.87)			
5 Most Severe Symptom Score, Month 3; n=37	-1.61 (± 1.76)			
5 Most Severe Symptom Score, Month 6; n=36	-1.69 (± 1.84)			
5 Most Severe Symptom Score, Month 12; n=37	-1.43 (± 1.72)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Subject Reported Quality of Life Measurements by The European Organization for Research and Treatment of Cancer - Quality of Life (QoL) Questionnaire (EORTC QLQ) Score After Switching to Dasatinib at Month 6 and 12

End point title	Change From Baseline in Subject Reported Quality of Life Measurements by The European Organization for Research and Treatment of Cancer - Quality of Life (QoL) Questionnaire (EORTC QLQ) Score After Switching to Dasatinib at Month 6 and 12

End point description:

The EORTC QLQ-C30 questionnaire was completed by study subjects to assess quality of life through nine multi-item scales: five functional scales (physical, role, cognitive, emotional and social functioning); three symptom scales (fatigue, pain and nausea/vomiting); and a global health status/QoL scale. Six single-item scales were included (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). All scales and single-item measures were evaluated at baseline and after switching to Dasatinib as an average raw score that was standardized by transformation, so that final scores were on a range in score from 0 to 100. A high score for a functional scale represented a healthy level of functioning, a high score for the global health status/QoL represented a high QoL, but a high score for a symptom scale represented a high level of problematic symptomatology. All treated subjects. Small "n" refers to total number of subjects that responded to the questionnaire.

End point type	Secondary

End point timeframe:

Baseline, Month 6 , Month 12

End point values	Dasatinib (100 mg)			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: Score on a scale				
arithmetic mean (standard deviation)				
Global Health Status/QOL, Month 6 (n=36)	0.46 (± 23.733)			
Global Health Status/QOL, Month 12 (n=35)	2.86 (± 27.782)			
Cognitive Functioning, Month 6 (n=35)	1.9 (± 20.119)			
Cognitive Functioning, Month 12 (n=35)	1.43 (± 18.245)			
Emotional Functioning, Month 6 (n=35)	11.19 (± 23.216)			
Emotional Functioning, Month 12 (n=35)	12.62 (± 25.595)			
Physical Functioning, Month 6 (n=36)	-1.67 (± 10.923)			
Physical Functioning, Month 12 (n=36)	0.74 (± 19.241)			
Role Functioning, Month 6 (n=36)	-4.17 (± 27.422)			
Role Functioning, Month 12 (n=36)	2.78 (± 23.401)			
Social Functioning, Month 6 (n=35)	13.81 (± 26.036)			
Social Functioning, Month 12 (n=35)	14.76 (± 24.512)			
Fatigue, Month 6 (n=36)	-6.79 (± 20.102)			
Fatigue, Month 12 (n=36)	-8.33 (± 21.639)			

Nausea and Vomiting, Month 6 (n=36)	-9.72 (± 31.966)			
Nausea and Vomiting, Month 12 (n=36)	-4.63 (± 30.76)			
Pain, Month 6 (n=36)	-2.78 (± 38.318)			
Pain, Month 12 (n=36)	-8.8 (± 25.35)			
Appetite Loss, Month 6 (n=35)	1.9 (± 29.085)			
Appetite Loss, Month 12 (n=36)	1.85 (± 29.755)			
Constipation, Month 6 (n=36)	-0.93 (± 28.156)			
Constipation, Month 12 (n=35)	8.57 (± 23.351)			
Diarrhoea, Month 6 (n=36)	0 (± 36.515)			
Diarrhoea, Month 12 (n=35)	-2.86 (± 40.722)			
Dyspnoea, Month 6 (n=36)	5.56 (± 36.947)			
Dyspnoea, Month 12 (n=36)	9.26 (± 39.53)			
Financial Difficulties, Month 6 (n=35)	-10.48 (± 21.038)			
Financial Difficulties, Month 12 (n=35)	-13.33 (± 18.436)			
Insomnia, Month 6 (n=36)	0.93 (± 42.528)			
Insomnia, Month 12 (n=36)	-1.85 (± 38.991)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With at least One AE, Discontinuations Due to AE, Treatment-related AE, Serious Adverse Event (SAE), Treatment-related SAE, or Death as an Outcome

End point title	Number of Subjects With at least One AE, Discontinuations Due to AE, Treatment-related AE, Serious Adverse Event (SAE), Treatment-related SAE, or Death as an Outcome

End point description:

SAE=a medical event that at any dose results in death, persistent or significant disability/incapacity, or drug dependency/abuse; is life-threatening, an important medical event, or a congenital anomaly/birth defect; or requires or prolongs hospitalization. AE=any new unfavorable symptom, sign, or disease or worsening of a preexisting condition that may not have a causal relationship with treatment. Treatment-related=having certain, probable, possible, or missing relationship to study drug, dasatinib. All treated subjects.

End point type	Secondary

End point timeframe:

SAEs: From screening period and within 30 days of discontinuation of dosing.
AEs: From first-treatment dose to 12 months

End point values	Dasatinib (100 mg)			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: Subjects				
At least 1 AE	37			
Discontinuations due to AE	3			
Treatment-related AEs	34			
SAEs	11			
Treatment-related SAEs	3			
Death	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With at Least 1 Imatinib-related Grade 1 or Grade 2 Chronic Adverse Events (AEs) That Improved Without Worsening Within 3 Months of Switching to Dasatinib

End point title	Percentage of Subjects With at Least 1 Imatinib-related Grade 1 or Grade 2 Chronic Adverse Events (AEs) That Improved Without Worsening Within 3 Months of Switching to Dasatinib

End point description:

The percentage of subjects is based on the number that had pre-existing Imatinib-related AEs. Subjects with reduction or improvement of at least 1 Imatinib-related Grade 1 or Grade 2 chronic AE, without a worsening of any Imatinib-related, chronic adverse events after dasatinib treatment were assessed. The severity of an adverse event is ranked based on grades that range from 1 to 4. Grade 1=Mild, Grade 2=Moderate, Grade 3=Severe, Grade 4= Potentially Life-threatening or disabling. Improved, AE grade reduced from Grade 2 to Grade 1. Worsened, Grade Increased. Confidence interval from Clopper-Pearson method. All treated subjects.

End point type	Secondary

End point timeframe:

3 months

End point values	Dasatinib (100 mg)			
Subject group type	Reporting group			
Number of subjects analysed	39[2]			
Units: Percentage of participants				
number (confidence interval 95%)	87.1 (72.5 to 95.7)			

Notes:

[2] - All treated subjects.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With a Major Molecular Response (MMR) and MR 4.5 After Switching to Dasatinib

End point title	Number of Subjects With a Major Molecular Response (MMR) and MR 4.5 After Switching to Dasatinib

End point description:

Molecular responses were assessed at 6 and 12 months after switching to dasatinib to determine if these baseline responses could be maintained. All treated subjects.

End point type	Other pre-specified

End point timeframe:

Month 6, Month 12

End point values	Dasatinib (100 mg)			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: Subjects				
MR4.5, Month 6	18			
MR4.5, Month 12	22			
MMR, Month 6	13			
MMR, Month 12	13			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Date of fist dose of study drug to 30 days post discontinuation of the last dose, up to October 2015	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups	
Reporting group title	Dasatinib (100 mg)
Reporting group description:	
Subjects that were previously on an imatinib therapy were treated with a 100 mg tablet of dasatinib taken orally once a day for up to 12 months while on study	

Serious adverse events	Dasatinib (100 mg)		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 39 (28.21%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Rib fracture			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Anal fissure			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhoids			

subjects affected / exposed	2 / 39 (5.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary arterial hypertension			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary oedema			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia			

subjects affected / exposed	2 / 39 (5.13%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Dasatinib (100 mg)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 39 (92.31%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Blood creatinine increased			
subjects affected / exposed	3 / 39 (7.69%)		
occurrences (all)	6		
Blood urea increased			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Cardiac disorders			
Left ventricular hypertrophy			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Pericardial effusion			
subjects affected / exposed	3 / 39 (7.69%)		
occurrences (all)	3		
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 39 (10.26%)		
occurrences (all)	5		
Headache			

subjects affected / exposed	15 / 39 (38.46%)		
occurrences (all)	19		
Paraesthesia			
subjects affected / exposed	3 / 39 (7.69%)		
occurrences (all)	4		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 39 (12.82%)		
occurrences (all)	13		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Face oedema			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	10 / 39 (25.64%)		
occurrences (all)	15		
General physical health deterioration			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	3		
Pyrexia			
subjects affected / exposed	6 / 39 (15.38%)		
occurrences (all)	6		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	4 / 39 (10.26%)		
occurrences (all)	4		
Diarrhoea			
subjects affected / exposed	11 / 39 (28.21%)		
occurrences (all)	16		
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Nausea			

subjects affected / exposed	8 / 39 (20.51%)		
occurrences (all)	8		
Vomiting			
subjects affected / exposed	3 / 39 (7.69%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 39 (15.38%)		
occurrences (all)	7		
Dysphonia			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Dyspnoea			
subjects affected / exposed	10 / 39 (25.64%)		
occurrences (all)	13		
Pleural effusion			
subjects affected / exposed	10 / 39 (25.64%)		
occurrences (all)	17		
Pulmonary hypertension			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Rhinitis allergic			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	4 / 39 (10.26%)		
occurrences (all)	5		
Rash			
subjects affected / exposed	10 / 39 (25.64%)		
occurrences (all)	13		
Psychiatric disorders			
Depression			
subjects affected / exposed	3 / 39 (7.69%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			

Arthralgia subjects affected / exposed occurrences (all) Musculoskeletal pain subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) Tendonitis subjects affected / exposed occurrences (all)	6 / 39 (15.38%) 9 3 / 39 (7.69%) 5 2 / 39 (5.13%) 3 3 / 39 (7.69%) 8 2 / 39 (5.13%) 2		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all)	3 / 39 (7.69%) 4		
Metabolism and nutrition disorders Hyperuricaemia subjects affected / exposed occurrences (all)	3 / 39 (7.69%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 August 2012	This protocol required subject to have the ability to complete patient reported outcome measure; the changes to this protocol in the Informed Consent and Inclusion/Exclusion Criteria sections reflected this requirement. Parameters regarding fluorescence in situ hybridization (FISH) testing were clarified and added to ensure accurate and feasible testing procedures for this study. The differences between disease progression and treatment failure were differentiated.
21 November 2012	The Purpose of this amendment was to: Chest x-rays are not considered to be standard of care in Germany. Therefore, this Amendment is designed to remove the requirement of pre-specified chest x-rays and allow the testing to be completed as clinically indicated. The exclusion criterion of pleural effusion is also changed to known pleural effusion as a result of this change. These changes will immediately affect all patients in the study sites located in Germany. Also, added the address in Belgium on the cover page.
09 October 2013	Based on an analysis of the BMS Dasatinib safety database (CARES) and a revision to an internal BMS directive related to "Women of Childbearing Potential (WOCBP) in clinical trials", this protocol was amended to adjust the frequency of pregnancy testing for sexually active female subjects of childbearing potential to monthly pregnancy testing. Additional changes related to this initiative were: • updated language related to WOCBP to harmonize with the new BMS directive including requiring 2 highly effective forms of birth control • defined highly effective forms of birth control • adjusted language related to sexually active fertile men with WOCBP partners and adapt the length of birth control to be used after the last dose of investigational product (90 days). Finally, an appendix was added to specify criteria for response required for study enrollment and clarifications were added to the time and events schedule.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported