Clinical trial results:
Dasatinib in Chronic Myelogenous Leukemia or Philadelphia Chromosome Positive Acute Lymphoblastic Leukemic Subjects Who are Experiencing Clinical Benefit on Current START, CA180039, or CA180043 Protocols: Long Term Safety and Efficacy Analysis.

Summary

EudraCT number	2007-003624-37
Trial protocol	DE BE IE GB IT FI ES HU
Global end of trial date	12 December 2014

Results information

Result version number	v1 (current)
This version publication date	01 July 2016
First version publication date	01 July 2016

Trial information

Trial identification

Sponsor protocol code	CA180-188

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00982488
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Bristol-Myers Squibb International Corporation, Chaussée de la Hulpe 185, Brussels, Belgium, 1170
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	12 December 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to determine the long term safety and tolerability of dasatinib.

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	11 October 2007
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	Poland: 16
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 13
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Finland: 2
Country: Number of subjects enrolled	Germany: 25
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	Ireland: 2
Country: Number of subjects enrolled	Italy: 17
Country: Number of subjects enrolled	Argentina: 6
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Brazil: 21
Country: Number of subjects enrolled	Canada: 19
Country: Number of subjects enrolled	Korea, Republic of: 11
Country: Number of subjects enrolled	Peru: 7
Country: Number of subjects enrolled	Russian Federation: 10
Country: Number of subjects enrolled	South Africa: 3
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	Thailand: 2
Country: Number of subjects enrolled	United States: 73

Worldwide total number of subjects	238
EEA total number of subjects	82

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)	170
From 65 to 84 years	68
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 58 sites in 20 countries.

Pre-assignment

Screening details:

A total of 238 subjects were enrolled: 200 with chronic phase chronic myelogenous leukemia (CML) and 38 with advanced phase disease (34 with accelerated phase CML, 3 with myeloid blast phase CML, and 1 with Philadelphia chromosome positive acute lymphoblastic leukemia.) All but 1 CML subject, who no longer met study criteria, received treatment.

Period 1

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

Blinding implementation details:

This study was an open-label study, hence no blinding was implemented.

Arms

Are arms mutually exclusive?	Yes
Arm title	Dasatinib 50 mg QD to 120 mg BID, Chronic Phase

Arm description:

Subjects with chronic phase disease were rolled over from previous studies CA180-039, CA180-043, and the SRC/ABL tyrosine kinase inhibition activity: Research trials (START). Subjects continued on the previous study dose of dasatinib, ranging from 50 mg once daily (QD) to 120 mg twice daily (BID). Dose escalations to optimize response and dose reductions for toxicity were permitted. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

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

Dosage and administration details:

Dasatinib 20-mg and 50-mg tablets were orally administered to meet daily dose of 20mg BID/40mg QD to maximum 100 mg BID/180 mg QD.

Arm title	Imatinib, 400 mg BID, Chronic Phase

Arm description:

Subjects with chronic phase disease received 400 mg of imatinib BID. Dose reduction to 600 mg/day (300 mg BID) was permitted, provided the subject had not previously received that dose prior to entry into CA180-017. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

Arm type	Experimental
Investigational medicinal product name	Imatinib
Investigational medicinal product code	
Other name	Gleevec/Glivec
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Imatinib 100-mg and 400-mg tablets were orally administered to meet daily dose of 300 or 400 mg.

Arm title	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, AP

Arm description:

Subjects with advanced phase disease, accelerated phase (AP) were rolled over from previous studies CA180-039, CA180-043, and the SRC/ABL tyrosine kinase inhibition activity: Research trials (START). Subjects continued on the previous study dose of dasatinib, ranging from 50 mg QD to 120 mg BID. Dose escalations to optimize response and dose reductions for toxicity were permitted. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

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

Dosage and administration details:

Dasatinib 20-mg and 50-mg tablets were orally administered to meet daily dose of 20mg BID/40mg QD to maximum 100 mg BID/180 mg QD.

Arm title	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, MPB

Arm description:

Subjects with advanced phase disease, myeloid blast phase (MPB), were rolled over from previous studies CA180-039, CA180-043, and the SRC/ABL tyrosine kinase inhibition activity: Research trials (START). Subjects continued on the previous study dose of dasatinib, ranging from 50 mg QD to 120 mg BID. Dose escalations to optimize response and dose reductions for toxicity were permitted. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

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

Dosage and administration details:

Dasatinib 20-mg and 50-mg tablets were orally administered to meet daily dose of 20mg BID/40mg QD to maximum 100 mg BID/180 mg QD.

Arm title	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, Ph+ ALL

Arm description:

Subjects with advanced phase disease, Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL), were rolled over from previous studies CA180-039, CA180-043, and the SRC/ABL tyrosine kinase inhibition activity: Research trials (START). Subjects continued on the previous study dose of dasatinib, ranging from 50 mg QD to 120 mg BID. Dose escalations to optimize response and dose reductions for toxicity were permitted. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

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

Dosage and administration details:

Dasatinib 20-mg and 50-mg tablets were orally administered to meet daily dose of 20mg BID/40mg QD to maximum 100 mg BID/180 mg QD.

Number of subjects in period 1[1]	Dasatinib 50 mg QD to 120 mg BID, Chronic Phase	Imatinib, 400 mg BID, Chronic Phase	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, AP
Started	185	14	34
Completed	0	0	0
Not completed	185	14	34
Consent withdrawn by subject	5	1	1
Disease progression	30	5	10
Poor/noncompliance	-	1	-
Study drug toxicity	34	1	6
Death	11	-	2
Maximum clinical benefit	1	1	1
Not specified	15	1	3
Adverse event unrelated to study drug	5	1	-
Stem cell transplant	2	-	-
Lost to follow-up	1	-	-
Administrative reason by sponsor	81	3	11

Number of subjects in period 1[1]	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, MPB	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, Ph+ ALL
Started	3	1
Completed	0	0
Not completed	3	1
Consent withdrawn by subject	-	-
Disease progression	1	1
Poor/noncompliance	-	-
Study drug toxicity	-	-
Death	-	-
Maximum clinical benefit	-	-
Not specified	1	-
Adverse event unrelated to study drug	-	-
Stem cell transplant	1	-
Lost to follow-up	-	-
Administrative reason by sponsor	-	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial as out of 238 subjects who were enrolled, 237 were treated. 1 subject no longer met study criteria.

Baseline characteristics

Reporting groups

Reporting group title	Dasatinib 50 mg QD to 120 mg BID, Chronic Phase

Reporting group description:

Subjects with chronic phase disease were rolled over from previous studies CA180-039, CA180-043, and the SRC/ABL tyrosine kinase inhibition activity: Research trials (START). Subjects continued on the previous study dose of dasatinib, ranging from 50 mg once daily (QD) to 120 mg twice daily (BID). Dose escalations to optimize response and dose reductions for toxicity were permitted. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

Reporting group title	Imatinib, 400 mg BID, Chronic Phase

Reporting group description:

Subjects with chronic phase disease received 400 mg of imatinib BID. Dose reduction to 600 mg/day (300 mg BID) was permitted, provided the subject had not previously received that dose prior to entry into CA180-017. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

Reporting group title	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, AP

Reporting group description:

Subjects with advanced phase disease, accelerated phase (AP) were rolled over from previous studies CA180-039, CA180-043, and the SRC/ABL tyrosine kinase inhibition activity: Research trials (START). Subjects continued on the previous study dose of dasatinib, ranging from 50 mg QD to 120 mg BID. Dose escalations to optimize response and dose reductions for toxicity were permitted. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

Reporting group title	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, MPB

Reporting group description:

Subjects with advanced phase disease, myeloid blast phase (MPB), were rolled over from previous studies CA180-039, CA180-043, and the SRC/ABL tyrosine kinase inhibition activity: Research trials (START). Subjects continued on the previous study dose of dasatinib, ranging from 50 mg QD to 120 mg BID. Dose escalations to optimize response and dose reductions for toxicity were permitted. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

Reporting group title	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, Ph+ ALL

Reporting group description:

Subjects with advanced phase disease, Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL), were rolled over from previous studies CA180-039, CA180-043, and the SRC/ABL tyrosine kinase inhibition activity: Research trials (START). Subjects continued on the previous study dose of dasatinib, ranging from 50 mg QD to 120 mg BID. Dose escalations to optimize response and dose reductions for toxicity were permitted. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

Reporting group values	Dasatinib 50 mg QD to 120 mg BID, Chronic Phase	Imatinib, 400 mg BID, Chronic Phase	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, AP
Number of subjects	185	14	34
Age categorical Units: Subjects			
Younger than 21 years	0	0	0
21-45 years	46	5	7
46-65 years	88	5	17
66-75 years	40	3	9
Older than 75 years	11	1	1
Age continuous Units: years			
arithmetic mean	55.7	51.5	56.3

standard deviation	± 13	± 15.8	± 11.2

Gender categorical Units: Subjects			
Female	91	6	15
Male	94	8	19
Race/Ethnicity, Customized Units: Subjects			
White	167	10	26
Black/African American	8	0	2
Asian	7	1	6
Other	3	3	0

Reporting group values	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, MPB	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, Ph+ ALL	Total
Number of subjects	3	1	237
Age categorical Units: Subjects			
Younger than 21 years	0	0	0
21-45 years	0	0	58
46-65 years	3	1	114
66-75 years	0	0	52
Older than 75 years	0	0	13
Age continuous Units: years			
arithmetic mean	57.3	62	
standard deviation	± 3.1	± 0	-
Gender categorical Units: Subjects			
Female	2	1	115
Male	1	0	122
Race/Ethnicity, Customized Units: Subjects			
White	2	1	206
Black/African American	0	0	10
Asian	0	0	14
Other	1	0	7

End points

End points reporting groups

Reporting group title	Dasatinib 50 mg QD to 120 mg BID, Chronic Phase

Reporting group description:

Subjects with chronic phase disease were rolled over from previous studies CA180-039, CA180-043, and the SRC/ABL tyrosine kinase inhibition activity: Research trials (START). Subjects continued on the previous study dose of dasatinib, ranging from 50 mg once daily (QD) to 120 mg twice daily (BID). Dose escalations to optimize response and dose reductions for toxicity were permitted. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

Reporting group title	Imatinib, 400 mg BID, Chronic Phase

Reporting group description:

Subjects with chronic phase disease received 400 mg of imatinib BID. Dose reduction to 600 mg/day (300 mg BID) was permitted, provided the subject had not previously received that dose prior to entry into CA180-017. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

Reporting group title	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, AP

Reporting group description:

Subjects with advanced phase disease, accelerated phase (AP) were rolled over from previous studies CA180-039, CA180-043, and the SRC/ABL tyrosine kinase inhibition activity: Research trials (START). Subjects continued on the previous study dose of dasatinib, ranging from 50 mg QD to 120 mg BID. Dose escalations to optimize response and dose reductions for toxicity were permitted. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

Reporting group title	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, MPB

Reporting group description:

Subjects with advanced phase disease, myeloid blast phase (MPB), were rolled over from previous studies CA180-039, CA180-043, and the SRC/ABL tyrosine kinase inhibition activity: Research trials (START). Subjects continued on the previous study dose of dasatinib, ranging from 50 mg QD to 120 mg BID. Dose escalations to optimize response and dose reductions for toxicity were permitted. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

Reporting group title	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, Ph+ ALL

Reporting group description:

Subjects with advanced phase disease, Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL), were rolled over from previous studies CA180-039, CA180-043, and the SRC/ABL tyrosine kinase inhibition activity: Research trials (START). Subjects continued on the previous study dose of dasatinib, ranging from 50 mg QD to 120 mg BID. Dose escalations to optimize response and dose reductions for toxicity were permitted. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

Primary: Number of Subjects With Serious Adverse Events (SAEs), Related SAEs, Adverse Events (AEs) Leading to Discontinuation, Related AEs Leading to Discontinuation, Related AEs, and Related AEs of Special Interest and Death

End point title	Number of Subjects With Serious Adverse Events (SAEs), Related SAEs, Adverse Events (AEs) Leading to Discontinuation, Related AEs Leading to Discontinuation, Related AEs, and Related AEs of Special Interest and Death[1]

End point description:

AE=any new unfavorable symptom, sign, or disease or worsening of a preexisting condition that may not have a causal relationship with treatment. 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. Related=drug-related; having certain, probable, possible, or unknown relationship to study drug. The analysis was performed in all the subjects who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Day 1 of treatment through a maximum of 82 months plus 30 days

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 summary statistics were planned for this outcome measure.

End point values	Dasatinib 50 mg QD to 120 mg BID, Chronic Phase	Imatinib, 400 mg BID, Chronic Phase	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, AP	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, MPB
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	185	14	34	3
Units: Subjects				
All deaths	22	0	4	0
Deaths within 30 days of last dose	9	0	2	0
SAEs	57	3	15	1
Drug-related SAEs	28	2	9	0
AEs leading to discontinuation	39	2	10	0
Drug-related AEs leading to discontinuation	29	1	8	0
Drug-related AEs	140	7	27	2
Drug-related AEs of special interest	111	4	21	1

End point values	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, Ph+ ALL			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Subjects				
All deaths	0			
Deaths within 30 days of last dose	0			
SAEs	1			
Drug-related SAEs	0			
AEs leading to discontinuation	1			
Drug-related AEs leading to discontinuation	0			
Drug-related AEs	0			
Drug-related AEs of special interest	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 of treatment through a maximum of 82 months plus 30 days

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Dasatinib 50 mg QD to 120 mg BID, Chronic Phase

Reporting group description:

Subjects with chronic phase disease were rolled over from previous studies CA180-039, CA180-043, and the SRC/ABL tyrosine kinase inhibition activity: Research trials (START). Subjects continued on the previous study dose of dasatinib, ranging from 50 mg once daily (QD) to 120 mg twice daily (BID). Dose escalations to optimize response and dose reductions for toxicity were permitted. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

Reporting group title	Imatinib, 400 mg BID, Chronic Phase

Reporting group description:

Subjects with chronic phase disease received 400 mg of imatinib BID. Dose reduction to 600 mg/day (300 mg BID) was permitted, provided the subject had not previously received that dose prior to entry into CA180-017. subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

Reporting group title	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, AP

Reporting group description:

Subjects with advanced phase disease, accelerated phase (AP) were rolled over from previous studies CA180-039, CA180-043, and the SRC/ABL tyrosine kinase inhibition activity: Research trials (START). Subjects continued on the previous study dose of dasatinib, ranging from 50 mg QD to 120 mg BID. Dose escalations to optimize response and dose reductions for toxicity were permitted. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

Reporting group title	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, MPB

Reporting group description:

Subjects with advanced phase disease, myeloid blast phase (MPB), were rolled over from previous studies CA180-039, CA180-043, and the SRC/ABL tyrosine kinase inhibition activity: Research trials (START). Subjects continued on the previous study dose of dasatinib, ranging from 50 mg QD to 120 mg BID. Dose escalations to optimize response and dose reductions for toxicity were permitted. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

Reporting group title	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, Ph+ ALL

Reporting group description:

Subjects with advanced phase disease, Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL), were rolled over from previous studies CA180-039, CA180-043, and the SRC/ABL tyrosine kinase inhibition activity: Research trials (START). Subjects continued on the previous study dose of dasatinib, ranging from 50 mg QD to 120 mg BID. Dose escalations to optimize response and dose reductions for toxicity were permitted. Subjects received study medication until disease progression, unacceptable toxicity, failure to serve subject's best interest, withdrawal of consent, or study closure.

Serious adverse events	Dasatinib 50 mg QD to 120 mg BID, Chronic Phase	Imatinib, 400 mg BID, Chronic Phase	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, AP
Total subjects affected by serious adverse events			
subjects affected / exposed	57 / 185 (30.81%)	3 / 14 (21.43%)	15 / 34 (44.12%)

number of deaths (all causes) number of deaths resulting from adverse events	22	0	4
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia recurrent			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	0 / 34 (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
Bladder cancer			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer recurrent			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (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
Tumour flare			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Breast cancer			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm			

subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Oophorectomy bilateral			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (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

Oedema peripheral			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Effusion			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pain			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	5 / 185 (2.70%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	1 / 5	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	2 / 185 (1.08%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Social circumstances			
Elderly			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal			

disorders			
Pulmonary arterial hypertension			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemothorax			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	13 / 185 (7.03%)	1 / 14 (7.14%)	3 / 34 (8.82%)
occurrences causally related to treatment / all	16 / 16	0 / 1	3 / 3
deaths causally related to treatment / all	2 / 2	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	3 / 185 (1.62%)	0 / 14 (0.00%)	3 / 34 (8.82%)
occurrences causally related to treatment / all	2 / 4	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	2 / 185 (1.08%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal septum perforation			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infiltration			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			

Depression			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Procedural haemorrhage			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transfusion reaction			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic rupture			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 185 (1.08%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bradyarrhythmia			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular dysfunction			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	2 / 185 (1.08%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Peripheral sensory neuropathy			
subjects affected / exposed	1 / 185 (0.54%)	1 / 14 (7.14%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIIth nerve paralysis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal artery occlusion			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vision blurred			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 185 (1.08%)	1 / 14 (7.14%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 4	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal haemorrhage			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pancreatitis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (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
Abdominal distension			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	2 / 185 (1.08%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Volvulus			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			

subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	2 / 185 (1.08%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 185 (0.00%)	1 / 14 (7.14%)	0 / 34 (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
Renal failure acute			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	0 / 34 (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
Musculoskeletal and connective tissue			

disorders			
Bone pain			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	0 / 34 (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
Spinal pain			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin pain			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cellulitis			
subjects affected / exposed	2 / 185 (1.08%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	3 / 185 (1.62%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	3 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	5 / 185 (2.70%)	0 / 14 (0.00%)	3 / 34 (8.82%)
occurrences causally related to treatment / all	2 / 7	0 / 0	1 / 3
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 1
Pseudomembranous colitis			
subjects affected / exposed	0 / 185 (0.00%)	1 / 14 (7.14%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	3 / 185 (1.62%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Hyperglycaemia			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obesity			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, MPB	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, Ph+ ALL	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	1 / 1 (100.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia recurrent			
subjects affected / exposed	0 / 3 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer recurrent			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm progression			

subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour flare			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Oophorectomy bilateral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Elderly			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal septum perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Procedural haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Transfusion reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic rupture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradyarrhythmia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIIth nerve paralysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			

Retinal artery occlusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			

subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Volvulus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	0 / 3 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomembranous colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Dasatinib 50 mg QD to 120 mg BID, Chronic Phase	Imatinib, 400 mg BID, Chronic Phase	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, AP
Total subjects affected by non-serious adverse events			
subjects affected / exposed	138 / 185 (74.59%)	10 / 14 (71.43%)	24 / 34 (70.59%)
Vascular disorders			
Hypertension			
subjects affected / exposed	12 / 185 (6.49%)	0 / 14 (0.00%)	3 / 34 (8.82%)
occurrences (all)	14	0	3
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	25 / 185 (13.51%)	1 / 14 (7.14%)	4 / 34 (11.76%)
occurrences (all)	32	1	4
Face oedema			
subjects affected / exposed	2 / 185 (1.08%)	1 / 14 (7.14%)	0 / 34 (0.00%)
occurrences (all)	2	1	0
Fatigue			
subjects affected / exposed	25 / 185 (13.51%)	1 / 14 (7.14%)	3 / 34 (8.82%)
occurrences (all)	27	1	3
Pyrexia			
subjects affected / exposed	15 / 185 (8.11%)	1 / 14 (7.14%)	1 / 34 (2.94%)
occurrences (all)	17	1	1
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	67 / 185 (36.22%)	1 / 14 (7.14%)	17 / 34 (50.00%)
occurrences (all)	93	1	19
Dyspnoea			
subjects affected / exposed	33 / 185 (17.84%)	0 / 14 (0.00%)	5 / 34 (14.71%)
occurrences (all)	44	0	9
Cough			
subjects affected / exposed	20 / 185 (10.81%)	0 / 14 (0.00%)	4 / 34 (11.76%)
occurrences (all)	21	0	4
Dyspnoea exertional			
subjects affected / exposed	8 / 185 (4.32%)	0 / 14 (0.00%)	3 / 34 (8.82%)
occurrences (all)	9	0	4
Psychiatric disorders			

Insomnia			
subjects affected / exposed	6 / 185 (3.24%)	1 / 14 (7.14%)	1 / 34 (2.94%)
occurrences (all)	6	1	1
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 185 (0.54%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 185 (0.00%)	1 / 14 (7.14%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Alanine aminotransferase increased			
subjects affected / exposed	2 / 185 (1.08%)	0 / 14 (0.00%)	2 / 34 (5.88%)
occurrences (all)	2	0	2
Blood fibrinogen decreased			
subjects affected / exposed	0 / 185 (0.00%)	1 / 14 (7.14%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Blood bilirubin			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Lipase increased			
subjects affected / exposed	0 / 185 (0.00%)	1 / 14 (7.14%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Diastolic dysfunction			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Nodal arrhythmia			
subjects affected / exposed	0 / 185 (0.00%)	1 / 14 (7.14%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	13 / 185 (7.03%)	0 / 14 (0.00%)	2 / 34 (5.88%)
occurrences (all)	15	0	2
Neuropathy peripheral			
subjects affected / exposed	2 / 185 (1.08%)	1 / 14 (7.14%)	0 / 34 (0.00%)
occurrences (all)	2	1	0

Headache			
subjects affected / exposed	14 / 185 (7.57%)	1 / 14 (7.14%)	1 / 34 (2.94%)
occurrences (all)	17	1	2
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	8 / 185 (4.32%)	1 / 14 (7.14%)	3 / 34 (8.82%)
occurrences (all)	17	3	4
Neutropenia			
subjects affected / exposed	8 / 185 (4.32%)	1 / 14 (7.14%)	3 / 34 (8.82%)
occurrences (all)	12	1	5
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	2 / 185 (1.08%)	1 / 14 (7.14%)	2 / 34 (5.88%)
occurrences (all)	2	2	2
Constipation			
subjects affected / exposed	9 / 185 (4.86%)	1 / 14 (7.14%)	1 / 34 (2.94%)
occurrences (all)	9	1	1
Abdominal distension			
subjects affected / exposed	3 / 185 (1.62%)	1 / 14 (7.14%)	2 / 34 (5.88%)
occurrences (all)	3	1	4
Diarrhoea			
subjects affected / exposed	19 / 185 (10.27%)	2 / 14 (14.29%)	2 / 34 (5.88%)
occurrences (all)	32	3	2
Nausea			
subjects affected / exposed	8 / 185 (4.32%)	0 / 14 (0.00%)	2 / 34 (5.88%)
occurrences (all)	10	0	2
Vomiting			
subjects affected / exposed	4 / 185 (2.16%)	3 / 14 (21.43%)	1 / 34 (2.94%)
occurrences (all)	4	4	1
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	2 / 185 (1.08%)	1 / 14 (7.14%)	0 / 34 (0.00%)
occurrences (all)	2	1	0
Rash			
subjects affected / exposed	31 / 185 (16.76%)	0 / 14 (0.00%)	4 / 34 (11.76%)
occurrences (all)	34	0	5
Pruritus			

subjects affected / exposed	5 / 185 (2.70%)	0 / 14 (0.00%)	2 / 34 (5.88%)
occurrences (all)	5	0	2
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	2 / 185 (1.08%)	1 / 14 (7.14%)	0 / 34 (0.00%)
occurrences (all)	3	1	0
Renal failure			
subjects affected / exposed	1 / 185 (0.54%)	1 / 14 (7.14%)	0 / 34 (0.00%)
occurrences (all)	1	1	0
Haematuria			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	12 / 185 (6.49%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences (all)	12	0	0
Osteoarthritis			
subjects affected / exposed	3 / 185 (1.62%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences (all)	3	0	0
Myalgia			
subjects affected / exposed	8 / 185 (4.32%)	1 / 14 (7.14%)	1 / 34 (2.94%)
occurrences (all)	10	1	1
Osteoporosis			
subjects affected / exposed	2 / 185 (1.08%)	1 / 14 (7.14%)	0 / 34 (0.00%)
occurrences (all)	2	1	0
Arthralgia			
subjects affected / exposed	14 / 185 (7.57%)	0 / 14 (0.00%)	1 / 34 (2.94%)
occurrences (all)	14	0	1
Back pain			
subjects affected / exposed	11 / 185 (5.95%)	1 / 14 (7.14%)	1 / 34 (2.94%)
occurrences (all)	11	1	1
Infections and infestations			
Viral infection			
subjects affected / exposed	2 / 185 (1.08%)	1 / 14 (7.14%)	0 / 34 (0.00%)
occurrences (all)	2	1	0
Gastroenteritis			

subjects affected / exposed	2 / 185 (1.08%)	1 / 14 (7.14%)	1 / 34 (2.94%)
occurrences (all)	3	1	1
Upper respiratory tract infection			
subjects affected / exposed	10 / 185 (5.41%)	1 / 14 (7.14%)	1 / 34 (2.94%)
occurrences (all)	15	1	1
Fungal skin infection			
subjects affected / exposed	1 / 185 (0.54%)	1 / 14 (7.14%)	0 / 34 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal infection			
subjects affected / exposed	1 / 185 (0.54%)	1 / 14 (7.14%)	0 / 34 (0.00%)
occurrences (all)	1	1	0
Localised infection			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Nasopharyngitis			
subjects affected / exposed	7 / 185 (3.78%)	1 / 14 (7.14%)	0 / 34 (0.00%)
occurrences (all)	7	1	0
Peritonsillar abscess			
subjects affected / exposed	0 / 185 (0.00%)	0 / 14 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	2 / 185 (1.08%)	1 / 14 (7.14%)	0 / 34 (0.00%)
occurrences (all)	2	1	0

Non-serious adverse events	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, MPB	Dasatinib, 50 mg QD to 120 mg BID, Advanced Phase, Ph+ ALL	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	0 / 1 (0.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	

Face oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Alanine aminotransferase increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood fibrinogen decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood bilirubin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Lipase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Diastolic dysfunction			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Nodal arrhythmia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Neuropathy peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			

Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Renal failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Haematuria			

subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Osteoarthritis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Osteoporosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Arthralgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Viral infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Fungal skin infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal infection			

subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Localised infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Peritonsillar abscess			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 December 2008	The required language regarding Serious Breach Identification and adverse event reporting were added.
24 November 2009	The international 24 hour telephone number was updated, quantitative polymerase chain reaction sample collection/analysis was removed, Imatinib dosing guidance for subjects with renal impairment was updated, and the serious adverse event submission process was updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported