Clinical trial results:
Phase 2 Placebo-controlled Double-blind Trial of Dasatinib Added to Gemcitabine for Subjects with Locally-advanced Pancreatic Cancer

Summary

EudraCT number	2010-024595-26
Trial protocol	BE HU GB AT DE CZ IE IT
Global end of trial date	21 April 2015

Results information

Result version number	v1 (current)
This version publication date	12 May 2016
First version publication date	12 May 2016

Trial information

Trial identification

Sponsor protocol code	287-11-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01395017
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Otsuka Pharmaceutical Development & Commercialization, Inc.
Sponsor organisation address	2440 Research Boulevard, Rockville, Maryland, United States, 20850
Public contact	Agnes Elekes, Otsuka Pharmaceutical Development & Commercialization, Inc. , +1 609-720-8453, agnes.elekes@otsuka-us.com
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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	13 June 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 November 2013
Global end of trial reached?	Yes
Global end of trial date	21 April 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to compare overall survival (OS) of participants with locally advanced pancreatic cancer (LAPC) who were randomized to receive dasatinib added to standard of care (gemcitabine [GEM]) versus standard of care (GEM) plus placebo.

Protection of trial subjects:

This trial was conducted in compliance with the protocol, International Conference on Harmonisation (ICH) Good Clinical Practice (GCP), and applicable local laws and regulatory requirements of the countries in which the trial was conducted, copies of the protocol, amendments, and informed consent form (ICF) were reviewed and approved by the governing institutional review board (IRB) or independent ethics committee (IEC) for each investigational site or country, as appropriate, prior to trial start or prior to implementation of the amendment at that site or country.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 August 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 16
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	Romania: 7
Country: Number of subjects enrolled	Russian Federation: 24
Country: Number of subjects enrolled	United States: 37
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	United Kingdom: 28
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Czech Republic: 10
Country: Number of subjects enrolled	France: 26
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Ireland: 6
Country: Number of subjects enrolled	Italy: 8
Worldwide total number of subjects	202
EEA total number of subjects	116

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)	95
From 65 to 84 years	104
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

202 participants were enrolled at 79 study sites in 15 countries.

Pre-assignment

Screening details:

Participants were randomly assigned in a 1:1 ratio to receive dasatinib + GEM or placebo + GEM. Participants were stratified at the time of randomization by Baseline Eastern Cooperative Oncology Group Performance Status (ECOG PS) (0 versus 1) and intent to receive radiotherapy (RT) (yes or no).

Period 1

Period 1 title	Overall Period (overall trial) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

To monitor participant safety, an independent data monitoring committee (IDMC) reviewed unblinded data. In addition, the IDMC reviewed unblinded data on the PFS endpoint after 151 Progression Free Survival events (disease progression, trial treatment discontinuation, or death) occurred. No study personnel directly involved with the study had access to unblinded data. The blind was not broken for any participant prior to database lock and overall study unblinding.

Arms

Are arms mutually exclusive?	Yes
Arm title	Dasatinib + GEM

Arm description:

GEM 1000 mg/m2 by intravenous (IV) infusion weekly for 3 weeks of a 4-week cycle plus dasatinib 100 mg by mouth once daily (QD).

Arm type	Active comparator
Investigational medicinal product name	Dasatinib
Investigational medicinal product code	SUB23159
Other name	Sprycel, Dasatinib monohydrate, BMS-35482
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

GEM 1000 mg/m2 by intravenous (IV) infusion weekly for 3 weeks of a 4-week cycle plus dasatinib 100 mg by mouth once daily (QD).

Arm title	Placebo + GEM

Arm description:

GEM 1000 mg/m2 by IV infusion weekly for 3 weeks of a 4-week cycle plus matched placebo by mouth QD.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

GEM 1000 mg/m2 by IV infusion weekly for 3 weeks of a 4-week cycle plus matched placebo by mouth QD.

Number of subjects in period 1	Dasatinib + GEM	Placebo + GEM
Started	100	102
Treated	98	101
Completed	0	0
Not completed	100	102
Physician decision	11	15
Consent withdrawn by subject	14	8
Disease progression	42	58
Death	4	3
Adverse event	26	12
Lost to follow-up	1	-
Sponsor discontinued study	1	4
Protocol deviation	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Dasatinib + GEM
Reporting group description:	
GEM 1000 mg/m2 by intravenous (IV) infusion weekly for 3 weeks of a 4-week cycle plus dasatinib 100 mg by mouth once daily (QD).	
Reporting group title	Placebo + GEM
Reporting group description:	
GEM 1000 mg/m2 by IV infusion weekly for 3 weeks of a 4-week cycle plus matched placebo by mouth QD.	

Reporting group values	Dasatinib + GEM	Placebo + GEM	Total
Number of subjects	100	102	202
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	47	48	95
From 65-84 years	51	53	104
85 years and over	2	1	3
Age continuous Units: years			
arithmetic mean	64.8	64.7	
standard deviation	± 9.1	± 9.6	-
Gender categorical Units: Subjects			
Female	43	56	99
Male	57	46	103

End points

End points reporting groups

Reporting group title	Dasatinib + GEM
Reporting group description:	
GEM 1000 mg/m2 by intravenous (IV) infusion weekly for 3 weeks of a 4-week cycle plus dasatinib 100 mg by mouth once daily (QD).	
Reporting group title	Placebo + GEM
Reporting group description:	
GEM 1000 mg/m2 by IV infusion weekly for 3 weeks of a 4-week cycle plus matched placebo by mouth QD.	

Primary: Overall Survival

End point title	Overall Survival
End point description:	
Overall survival (OS) is the time from randomization until time of death from any cause by 02 December 2013. The intent-to-treat (ITT) data was used, which was composed of all randomized participants.	
End point type	Primary
End point timeframe:	
From randomization until date of death from any cause by 02 December 2013	

End point values	Dasatinib + GEM	Placebo + GEM		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	102		
Units: Days				
median (confidence interval 95%)	375 (310 to 462)	393 (356 to 467)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Using a 1-sided alpha=0.2, a population of 200 participants (100 GEM plus dasatinib and 100 GEM plus placebo) has 79% power to show an increase in median OS from 10 to 13.3 months (hazard ratio [HR] =0.75, assuming analysis of 135 deaths).	
Comparison groups	Dasatinib + GEM v Placebo + GEM
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.3864 [2]
Method	Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.19

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.65

Notes:

[1] - Adjusting for baseline factors - treatment, ECOG PS, region, CA19-9 level (< 1000 IU/mL or >/=1000 IU/mL), and RT during trial (yes or no).
[2] - The log-rank test was used to test OS. As a sensitivity analysis, HR and its confidence interval was also provided for OS using the Cox proportional hazard model.

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS - time from randomization to unequivocal local or distant disease progression, death or discontinuation from trial for any reason by 02 December 2013. Progression events were determined according to Response Evaluation Criteria in Solid Tumor (RECIST) 1.1 every 8 weeks. The ITT data was used, which was composed of all randomized participants.

End point type	Secondary

End point timeframe:

Time from randomization to earliest PFS event by 02 December 2013

End point values	Dasatinib + GEM	Placebo + GEM		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	102		
Units: Days				
median (confidence interval 95%)	167 (114 to 212)	166 (158 to 199)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Trial has 88% power to show a median PFS increase from 5 to 7 months (with 1-sided alpha=0.15, total 176 events, HR=0.714).

Comparison groups	Dasatinib + GEM v Placebo + GEM
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.6761 [4]
Method	Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.34

Notes:

[3] - Adjusting for baseline factors: treatment, ECOG PS, region, CA19-9 level (< 1000 IU/mL or >/=1000 IU/mL), and RT during trial (yes or no).

[4] - The log-rank test was used to test PFS. As a sensitivity analysis, HR and its confidence interval was also provided for PFS using the Cox proportional hazard model.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from randomization throughout each treatment cycle to final study visit. Follow-up visits conducted until all ongoing AEs resolved or clinically stable.

Adverse event reporting additional description:

The safety data set (participants who received at least one dose of study treatment) included 98 participants in the Dasatinib + GEM group and 101 participants in the placebo + GEM group.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Dasatinib + GEM

Reporting group description:

GEM 1000 mg/m2 by IV infusion weekly for 3 weeks of a 4-week cycle plus dasatinib 100 mg by mouth QD.

Reporting group title	Placebo + GEM

Reporting group description:

GEM 1000 mg/m2 by IV infusion weekly for 3 weeks of a 4-week cycle plus matched placebo by mouth QD.

Serious adverse events	Dasatinib + GEM	Placebo + GEM	
Total subjects affected by serious adverse events			
subjects affected / exposed	53 / 98 (54.08%)	48 / 101 (47.52%)	
number of deaths (all causes)	9	10	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	2 / 98 (2.04%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Metastases to bone			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tumour haemorrhage			

subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device occlusion			
subjects affected / exposed	5 / 98 (5.10%)	5 / 101 (4.95%)	
occurrences causally related to treatment / all	5 / 5	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	

General physical health deterioration			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthermia			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oedema			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	3 / 98 (3.06%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 98 (1.02%)	4 / 101 (3.96%)	
occurrences causally related to treatment / all	1 / 1	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stent malfunction			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			

subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 98 (1.02%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthmatic crisis			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	2 / 98 (2.04%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	4 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			

subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	6 / 98 (6.12%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	6 / 6	3 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary arterial hypertension			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			

subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chemical peritonitis			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal stoma complication			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Head injury			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural bile leak			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Pyloric stenosis			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Cardiac failure			
subjects affected / exposed	4 / 98 (4.08%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	4 / 4	2 / 2	
deaths causally related to treatment / all	1 / 2	0 / 1	

Cardiac failure acute			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiomyopathy			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sick sinus syndrome			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 98 (3.06%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	4 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 98 (3.06%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 98 (1.02%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ascites			
subjects affected / exposed	2 / 98 (2.04%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	2 / 2	2 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Constipation			
subjects affected / exposed	2 / 98 (2.04%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	3 / 98 (3.06%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal stenosis			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer perforation			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 98 (1.02%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nausea			

subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction gastric			
subjects affected / exposed	3 / 98 (3.06%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic necrosis			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestine obstruction			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	3 / 98 (3.06%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	4 / 4	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	4 / 98 (4.08%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	4 / 4	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stenosis			
subjects affected / exposed	2 / 98 (2.04%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	4 / 98 (4.08%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	4 / 4	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			

subjects affected / exposed	1 / 98 (1.02%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatotoxicity			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	5 / 98 (5.10%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	5 / 5	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	2 / 98 (2.04%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrolytic migratory erythema			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic skin eruption			

subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal failure acute			
subjects affected / exposed	1 / 98 (1.02%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteonecrosis			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary sepsis			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Biliary tract infection			
subjects affected / exposed	2 / 98 (2.04%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	2 / 98 (2.04%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia infection			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abcess			
subjects affected / exposed	1 / 98 (1.02%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			

subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 98 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia			
subjects affected / exposed	3 / 98 (3.06%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sepsis			
subjects affected / exposed	2 / 98 (2.04%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal infection			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	3 / 98 (3.06%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 98 (1.02%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	2 / 98 (2.04%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	2 / 98 (2.04%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fluid retention			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 98 (0.00%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	1 / 98 (1.02%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	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 + GEM	Placebo + GEM	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	93 / 98 (94.90%)	98 / 101 (97.03%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 98 (4.08%)	10 / 101 (9.90%)	
occurrences (all)	5	10	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	17 / 98 (17.35%)	16 / 101 (15.84%)	
occurrences (all)	35	26	
Chest pain			
subjects affected / exposed	2 / 98 (2.04%)	7 / 101 (6.93%)	
occurrences (all)	2	7	
Chills			
subjects affected / exposed	6 / 98 (6.12%)	4 / 101 (3.96%)	
occurrences (all)	6	7	
Face oedema			
subjects affected / exposed	5 / 98 (5.10%)	1 / 101 (0.99%)	
occurrences (all)	5	1	
Fatigue			
subjects affected / exposed	50 / 98 (51.02%)	46 / 101 (45.54%)	
occurrences (all)	179	102	
Oedema peripheral			
subjects affected / exposed	32 / 98 (32.65%)	22 / 101 (21.78%)	
occurrences (all)	67	30	
Pain			
subjects affected / exposed	2 / 98 (2.04%)	8 / 101 (7.92%)	
occurrences (all)	2	9	
Pyrexia			
subjects affected / exposed	22 / 98 (22.45%)	27 / 101 (26.73%)	
occurrences (all)	49	56	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	14 / 98 (14.29%)	13 / 101 (12.87%)	
occurrences (all)	20	13	

Dyspnoea			
subjects affected / exposed	25 / 98 (25.51%)	19 / 101 (18.81%)	
occurrences (all)	38	34	
Pleural effusion			
subjects affected / exposed	20 / 98 (20.41%)	5 / 101 (4.95%)	
occurrences (all)	28	6	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	10 / 98 (10.20%)	4 / 101 (3.96%)	
occurrences (all)	10	4	
Depression			
subjects affected / exposed	6 / 98 (6.12%)	5 / 101 (4.95%)	
occurrences (all)	6	5	
Insomnia			
subjects affected / exposed	12 / 98 (12.24%)	14 / 101 (13.86%)	
occurrences (all)	13	14	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	22 / 98 (22.45%)	14 / 101 (13.86%)	
occurrences (all)	60	20	
Blood alkaline phosphatase increased			
subjects affected / exposed	15 / 98 (15.31%)	8 / 101 (7.92%)	
occurrences (all)	36	18	
Blood bilirubin increased			
subjects affected / exposed	13 / 98 (13.27%)	6 / 101 (5.94%)	
occurrences (all)	19	12	
Gamma glutamyltransferase increased			
subjects affected / exposed	5 / 98 (5.10%)	1 / 101 (0.99%)	
occurrences (all)	12	1	
Haemaglobin decreased			
subjects affected / exposed	5 / 98 (5.10%)	6 / 101 (5.94%)	
occurrences (all)	11	23	
Neutrophil count decreased			
subjects affected / exposed	6 / 98 (6.12%)	5 / 101 (4.95%)	
occurrences (all)	16	12	
Platelet count decreased			

subjects affected / exposed	7 / 98 (7.14%)	4 / 101 (3.96%)	
occurrences (all)	14	4	
Weight decreased			
subjects affected / exposed	21 / 98 (21.43%)	11 / 101 (10.89%)	
occurrences (all)	29	14	
White blood cell count decreased			
subjects affected / exposed	8 / 98 (8.16%)	2 / 101 (1.98%)	
occurrences (all)	43	8	
Aspartate aminotransferase increased			
subjects affected / exposed	16 / 98 (16.33%)	11 / 101 (10.89%)	
occurrences (all)	35	19	
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 98 (4.08%)	11 / 101 (10.89%)	
occurrences (all)	5	15	
Dysgeusia			
subjects affected / exposed	12 / 98 (12.24%)	6 / 101 (5.94%)	
occurrences (all)	22	13	
Headache			
subjects affected / exposed	12 / 98 (12.24%)	9 / 101 (8.91%)	
occurrences (all)	15	10	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	50 / 98 (51.02%)	28 / 101 (27.72%)	
occurrences (all)	139	74	
Leukopenia			
subjects affected / exposed	8 / 98 (8.16%)	13 / 101 (12.87%)	
occurrences (all)	31	29	
Lymphopenia			
subjects affected / exposed	5 / 98 (5.10%)	7 / 101 (6.93%)	
occurrences (all)	26	36	
Neutropenia			
subjects affected / exposed	53 / 98 (54.08%)	49 / 101 (48.51%)	
occurrences (all)	176	194	
Thrombocytopenia			

subjects affected / exposed	38 / 98 (38.78%)	39 / 101 (38.61%)	
occurrences (all)	122	134	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	33 / 98 (33.67%)	36 / 101 (35.64%)	
occurrences (all)	73	67	
Abdominal pain upper			
subjects affected / exposed	10 / 98 (10.20%)	18 / 101 (17.82%)	
occurrences (all)	18	26	
Ascites			
subjects affected / exposed	8 / 98 (8.16%)	6 / 101 (5.94%)	
occurrences (all)	16	9	
Constipation			
subjects affected / exposed	33 / 98 (33.67%)	28 / 101 (27.72%)	
occurrences (all)	46	39	
Diarrhoea			
subjects affected / exposed	41 / 98 (41.84%)	29 / 101 (28.71%)	
occurrences (all)	122	69	
Dry mouth			
subjects affected / exposed	5 / 98 (5.10%)	6 / 101 (5.94%)	
occurrences (all)	5	6	
Dyspepsia			
subjects affected / exposed	9 / 98 (9.18%)	7 / 101 (6.93%)	
occurrences (all)	16	9	
Flatulence			
subjects affected / exposed	6 / 98 (6.12%)	11 / 101 (10.89%)	
occurrences (all)	6	12	
Nausea			
subjects affected / exposed	65 / 98 (66.33%)	49 / 101 (48.51%)	
occurrences (all)	139	89	
Stomatitis			
subjects affected / exposed	9 / 98 (9.18%)	8 / 101 (7.92%)	
occurrences (all)	13	10	
Vomiting			
subjects affected / exposed	40 / 98 (40.82%)	34 / 101 (33.66%)	
occurrences (all)	95	54	

Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	3 / 98 (3.06%)	7 / 101 (6.93%)	
occurrences (all)	6	13	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	10 / 98 (10.20%)	7 / 101 (6.93%)	
occurrences (all)	10	8	
Dry skin			
subjects affected / exposed	5 / 98 (5.10%)	3 / 101 (2.97%)	
occurrences (all)	7	3	
Erythema			
subjects affected / exposed	5 / 98 (5.10%)	3 / 101 (2.97%)	
occurrences (all)	7	3	
Night sweats			
subjects affected / exposed	6 / 98 (6.12%)	2 / 101 (1.98%)	
occurrences (all)	6	2	
Pruritus			
subjects affected / exposed	6 / 98 (6.12%)	9 / 101 (8.91%)	
occurrences (all)	8	12	
Rash			
subjects affected / exposed	20 / 98 (20.41%)	14 / 101 (13.86%)	
occurrences (all)	28	20	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 98 (3.06%)	6 / 101 (5.94%)	
occurrences (all)	8	16	
Back pain			
subjects affected / exposed	8 / 98 (8.16%)	16 / 101 (15.84%)	
occurrences (all)	10	19	
Muscloskeletal pain			
subjects affected / exposed	1 / 98 (1.02%)	6 / 101 (5.94%)	
occurrences (all)	1	7	
Pain in extremity			
subjects affected / exposed	10 / 98 (10.20%)	5 / 101 (4.95%)	
occurrences (all)	10	6	

Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 98 (7.14%)	5 / 101 (4.95%)	
occurrences (all)	9	5	
Oral candidiasis			
subjects affected / exposed	7 / 98 (7.14%)	5 / 101 (4.95%)	
occurrences (all)	8	5	
Upper respiratory tract infection			
subjects affected / exposed	7 / 98 (7.14%)	3 / 101 (2.97%)	
occurrences (all)	7	3	
Urinary tract infection			
subjects affected / exposed	6 / 98 (6.12%)	1 / 101 (0.99%)	
occurrences (all)	9	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	48 / 98 (48.98%)	23 / 101 (22.77%)	
occurrences (all)	82	48	
Hyperglycaemia			
subjects affected / exposed	9 / 98 (9.18%)	6 / 101 (5.94%)	
occurrences (all)	31	15	
Hypokalaemia			
subjects affected / exposed	12 / 98 (12.24%)	10 / 101 (9.90%)	
occurrences (all)	19	15	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 February 2013	This protocol amendment corrects some typographical errors, updates some definitions in section 5.1, provides clarification on blood sampling for CA19-9, provides clarification on PFS assessments, states that the investigator would now directly access the Interactive voice/Web response system (IVRS/IWRS) system should there be a need to break the blind for a participant for safety reasons, and now correctly states that the IDMC board would not share their findings on efficacy with the sponsor at the interim analysis.
08 November 2013	This protocol amendment removes all references to commercial supply of dasatinib and adds a possible additional analysis once deaths were recorded for up to 90% of participants.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported