Clinical trial results:
A Phase 2 Multi-Center, Historically-Controlled Study of Dasatinib Added to Standard Chemotherapy in Pediatric Patients with Newly Diagnosed Philadelphia Chromosome Positive Acute Lymphoblastic Leukemia

Summary

EudraCT number	2011-001123-20
Trial protocol	IT GB Outside EU/EEA
Global end of trial date	01 June 2021

Results information

Result version number	v2 (current)
This version publication date	24 November 2021
First version publication date	10 June 2018
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CA180-372

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, 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)	Yes
EMA paediatric investigation plan number(s)	EMEA-000567-PIP09-05
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?	Yes

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	28 May 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 May 2017
Global end of trial reached?	Yes
Global end of trial date	01 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the 3-year efficacy based on EFS of dasatinib plus chemotherapy with external historical controls, in hierarchical order, as follows: - Superiority over chemotherapy alone of AIEOP-BFM 2000 - Non-inferiority to continuous imatinib plus chemotherapy of the amended EsPhALL trial - Superiority over continuous imatinib plus chemotherapy of the amended EsPhALL trial

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	13 April 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	United Kingdom: 12
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	United States: 76
Worldwide total number of subjects	106
EEA total number of subjects	13

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	4

months)	
Children (2-11 years)	67
Adolescents (12-17 years)	35
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

106 participants were treated with dasatinib (82 participants received dasatinib in the tablet form exclusively and 24 participants received either tablet and/or PFOS).

Period 1

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

Arms

Arm title	Dasatinib Cohort

Arm description:

Children and adolescents newly diagnosed with Philadelphia chromosome positive acute lymphocytic leukemia (Ph+ ALL) treated with standard multiagent chemotherapy and Dasatinib (either in tablets or Powder For Oral Suspension (PFOS)) at a dose of 60 mg/m2 daily.

Arm type	Experimental
Investigational medicinal product name	Dasatinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for oral suspension
Routes of administration	Oral use

Dosage and administration details:

60 mg/m2 daily

Investigational medicinal product name	Dasatinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

60 mg/m2 daily

Number of subjects in period 1	Dasatinib Cohort
Started	106
Completed	78
Not completed	28
Adverse event, serious fatal	2
Consent withdrawn by subject	4
Adverse event, non-fatal	8
Other reasons	9
Study Drug Toxicity	2

Lack of efficacy	3

Baseline characteristics

Reporting groups	
Reporting group title	Dasatinib Cohort
Reporting group description:	
Children and adolescents newly diagnosed with Philadelphia chromosome positive acute lymphocytic leukemia (Ph+ ALL) treated with standard multiagent chemotherapy and Dasatinib (either in tablets or Powder For Oral Suspension (PFOS)) at a dose of 60 mg/m2 daily.	

Reporting group values	Dasatinib Cohort	Total	
Number of subjects	106	106	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	4	4	
Children (2-11 years)	67	67	
Adolescents (12-17 years)	35	35	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	9.29		
standard deviation	± 4.467	-	
Sex: Female, Male Units: Participants			
Female	49	49	
Male	57	57	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	5	5	
Native Hawaiian or Other Pacific Islander	1	1	
Black or African American	13	13	
White	85	85	
More than one race	0	0	
Unknown or Not Reported	1	1	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	24	24	
Not Hispanic or Latino	55	55	
Unknown or Not Reported	27	27	

End points

End points reporting groups

Reporting group title	Dasatinib Cohort

Reporting group description:

Children and adolescents newly diagnosed with Philadelphia chromosome positive acute lymphocytic leukemia (Ph+ ALL) treated with standard multiagent chemotherapy and Dasatinib (either in tablets or Powder For Oral Suspension (PFOS)) at a dose of 60 mg/m2 daily.

Subject analysis set title	Historical Controls
Subject analysis set type	Per protocol

Subject analysis set description:

This subset represents the totality of historical controls used for the statistical analyses.
The number of subjects are:
AIEOP-BFM: N=61
EsPhALL: N=137
COG AALL0031: N=56

Primary: 3-year Event-free Survival (EFS) Rate

End point title	3-year Event-free Survival (EFS) Rate

End point description:

3-year EFS rate is defined as the percentage of participants without event after 3 years since the start of study treatment. Events for EFS are defined as ANY first one of the following: · Lack of complete response in bone marrow · Relapse at any site · Development of second malignant neoplasm · Death from any cause

End point type	Primary

End point timeframe:

From first dose to 3 years following first dose

End point values	Dasatinib Cohort	Historical Controls		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	106	1[1]		
Units: Percentage of Participants				
number (confidence interval 90%)	66.0 (57.7 to 73.7)	99999 (99999 to 99999)		

Notes:

[1] - Historical controls were used as a comparator for statistical analyses

Statistical analyses

Statistical analysis title	EFS rate_1

Statistical analysis description:

Difference in 3-year binomial EFS rate in all treated participants (dasatinib plus chemotherapy) vs. chemotherapy alone in AIEOP-BFM 2000 historical control

Comparison groups	Dasatinib Cohort v Historical Controls

Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.032 [2]
Method	Chi-squared
Parameter estimate	Estimate of Difference
Point estimate	16.86
Confidence interval	
level	90 %
sides	2-sided
lower limit	3.9
upper limit	29.8

Notes:

[2] - Superiority test versus AIEOP-BFM 2000

Statistical analysis title	EFS rate_2

Statistical analysis description:

Difference in 3-year binomial EFS rate for all treated participants (dasatinib plus chemotherapy) vs. continuous imatinib plus chemotherapy in the Amended EsPhALL Trial Historical Control

Comparison groups	Dasatinib Cohort v Historical Controls
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.271 [3]
Method	Chi-squared
Parameter estimate	Estimate of difference
Point estimate	6.91
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.3
upper limit	17.2

Notes:

[3] - Superiority test versus EsPhALL

Statistical analysis title	EFS rate_3
Comparison groups	Dasatinib Cohort v Historical Controls
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.157
Method	Chi-squared
Parameter estimate	Estimate of difference
Point estimate	-10.75
Confidence interval	
level	90 %
sides	2-sided
lower limit	-22.7
upper limit	1.2

Secondary: Complete Remission Rate

End point title	Complete Remission Rate

End point description:

Complete Remission rate is defined as the percentage of participants achieving a complete remission, i.e. < 5% lymphoblasts in bone marrow and in CSF, with no evidence of other extramedullary disease. Complete remission will be assessed at the end of Induction IA, end of induction IB and end of the consolidation period for all treated participants.

End point type	Secondary

End point timeframe:

From first dose to End of Induction Period Ia (up to 5 weeks) or Ib (up to 9 weeks) or End of Consolidation Period (up to 22 weeks)

End point values	Dasatinib Cohort			
Subject group type	Reporting group			
Number of subjects analysed	106			
Units: Percentage of Partcipants				
number (not applicable)				
End of Induction period Ia	65.1			
End of Induction period Ib	88.7			
End of Consolidation period	93.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Adverse Events

End point title	Number of Participants Experiencing Adverse Events

End point description:

Number of participants experiencing different types of all causality all grade adverse events

End point type	Secondary

End point timeframe:

From first dose to 100 days following last dose (up to approximately 23 months)

End point values	Dasatinib Cohort			
Subject group type	Reporting group			
Number of subjects analysed	106			
Units: Participants				
Adverse Events (AEs)	106			
Drug-related AEs	88			
AEs leading to discontinuation	7			

Serious Adverse Events (SAEs)	101			
Deaths	15			

Statistical analyses

No statistical analyses for this end point

Secondary: Event-Free Survival (EFS) Rate (Kaplan-Meier Estimates)

End point title	Event-Free Survival (EFS) Rate (Kaplan-Meier Estimates)

End point description:

Overall estimation of the EFS of dasatinib plus chemotherapy was performed utilizing the Kaplan-Meier (KM) Product Limit method. The 3-year and 5-year EFS rates were computed with the corresponding 95% CI's using Greenwood's formula. Analyses of EFS included KM plots with number of patients at risk. Participants who neither relapse nor die or who are lost to follow-up were censored on the date of their last bone marrow, CSF assessment or physical exam, whichever occurred last.

End point type	Secondary

End point timeframe:

From first dose to 3 years or 5 years following first dose

End point values	Dasatinib Cohort			
Subject group type	Reporting group			
Number of subjects analysed	106			
Units: Percentage of Participants				
number (confidence interval 95%)				
3-year EFS Estimate	65.5 (55.5 to 73.7)			
5-year EFS Estimate	53.1 (42.8 to 62.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Negative for Minimal Residual Disease (MRD)

End point title	Percentage of Participants Negative for Minimal Residual Disease (MRD)

End point description:

MRD was by real-time qPCR for clone-specific immunoglobulin and T-cell receptor gene rearrangements (IG/TCR). Participants were declared as MRD negative if the MRD level is undetectable providing the assay lower limit of quantification is at least 0.1%

End point type	Secondary

End point timeframe:

From first dose to End of Induction Period Ia (up to 5 weeks) or Ib (up to 9 weeks) or End of Consolidation Period (up to 22 weeks)

End point values	Dasatinib Cohort			
Subject group type	Reporting group			
Number of subjects analysed	106			
Units: Percentage of Participants				
number (confidence interval 95%)				
End of Induction period Ia	28.3 (19.98 to 37.88)			
End of Induction period Ib	52.8 (42.89 to 62.60)			
End of Consolidation period	71.7 (62.12 to 80.02)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with BCR-ABL Mutations at Baseline and at Time of Disease Progression or Relapse

End point title	Percentage of Participants with BCR-ABL Mutations at Baseline and at Time of Disease Progression or Relapse

End point description:

A BCR-ABL mutation is defined as the presence of a detectable amino acid substitution in the ABL kinase domain, assessed by Real-time quantitative PCR.

End point type	Secondary

End point timeframe:

At baseline (prior to start of study treatment) and at disease progression or relapse (up to approximately 3 years)

End point values	Dasatinib Cohort			
Subject group type	Reporting group			
Number of subjects analysed	106			
Units: Percentage of participants				
number (not applicable)				
At Baseline	1.3			
At Disease Progression or Relapse	6.5			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All cause mortality was assessed from first dose to study completion.
SAEs and Other AEs were assessed from first dose to 100 days following last dose (up to approximately 23 months).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	DASATINIB

Reporting group description:

Subjects with Philadelphia Chromosome Positive Acute Lymphoblastic Leukemia (Ph+ ALL) were administered Dasatinib tablet (approximately equivalent to 100 mg daily for an adult) or Powder for oral suspension (PFOS) (who are unable to swallow tablets were administered Dasatinib PFOS 10 mg/milliliter) at a dose of 60 milligrams per square meter of body surface area or once daily orally in combination with standard chemotherapy and followed up for 3 years.

Serious adverse events	DASATINIB		
Total subjects affected by serious adverse events			
subjects affected / exposed	101 / 106 (95.28%)		
number of deaths (all causes)	21		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACUTE LYMPHOCYTIC LEUKAEMIA			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
ASTROCYTOMA			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LEUKAEMIA RECURRENT			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
EMBOLISM			

subjects affected / exposed	3 / 106 (2.83%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
HYPERTENSION				
subjects affected / exposed	7 / 106 (6.60%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 0			
HYPOTENSION				
subjects affected / exposed	22 / 106 (20.75%)			
occurrences causally related to treatment / all	2 / 29			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
CHILLS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
DEVICE RELATED THROMBOSIS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
INFLUENZA LIKE ILLNESS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
LOCALISED OEDEMA				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
MUCOSAL INFLAMMATION				
subjects affected / exposed	18 / 106 (16.98%)			
occurrences causally related to treatment / all	2 / 24			
deaths causally related to treatment / all	0 / 0			
NON-CARDIAC CHEST PAIN				

subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
OEDEMA				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
OEDEMA PERIPHERAL				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
PAIN				
subjects affected / exposed	3 / 106 (2.83%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
PYREXIA				
subjects affected / exposed	52 / 106 (49.06%)			
occurrences causally related to treatment / all	14 / 132			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
ANAPHYLACTIC REACTION				
subjects affected / exposed	7 / 106 (6.60%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 0			
DRUG HYPERSENSITIVITY				
subjects affected / exposed	7 / 106 (6.60%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
OEDEMA GENITAL				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Respiratory, thoracic and mediastinal disorders			
CHYLOTHORAX			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
COUGH			
subjects affected / exposed	8 / 106 (7.55%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
DYSPNOEA			
subjects affected / exposed	4 / 106 (3.77%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
EPISTAXIS			
subjects affected / exposed	2 / 106 (1.89%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
HAEMOTHORAX			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
HYPOXIA			
subjects affected / exposed	7 / 106 (6.60%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
PLEURAL EFFUSION			
subjects affected / exposed	9 / 106 (8.49%)		
occurrences causally related to treatment / all	3 / 11		
deaths causally related to treatment / all	0 / 0		
PLEURITIC PAIN			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

PNEUMONITIS				
subjects affected / exposed	3 / 106 (2.83%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
PULMONARY OEDEMA				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
RESPIRATORY DISTRESS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
STRIDOR				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
ANXIETY				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
DELIRIUM				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
PERSONALITY CHANGE				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
ALANINE AMINOTRANSFERASE INCREASED				
subjects affected / exposed	5 / 106 (4.72%)			
occurrences causally related to treatment / all	2 / 5			
deaths causally related to treatment / all	0 / 0			

ASPARTATE AMINOTRANSFERASE INCREASED				
subjects affected / exposed	3 / 106 (2.83%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
BLOOD BILIRUBIN INCREASED				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
BLOOD CREATININE INCREASED				
subjects affected / exposed	7 / 106 (6.60%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
BLOOD CULTURE POSITIVE				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
DRUG CLEARANCE DECREASED				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
ENTEROVIRUS TEST POSITIVE				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
NEUTROPHIL COUNT DECREASED				
subjects affected / exposed	9 / 106 (8.49%)			
occurrences causally related to treatment / all	7 / 12			
deaths causally related to treatment / all	0 / 0			
PLATELET COUNT DECREASED				
subjects affected / exposed	7 / 106 (6.60%)			
occurrences causally related to treatment / all	1 / 8			
deaths causally related to treatment / all	0 / 0			
TRANSAMINASES INCREASED				

subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
TROPONIN I INCREASED				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
URINE OUTPUT DECREASED				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
VIRAL TEST				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
WEIGHT DECREASED				
subjects affected / exposed	3 / 106 (2.83%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
WHITE BLOOD CELL COUNT DECREASED				
subjects affected / exposed	6 / 106 (5.66%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 0			
WHITE BLOOD CELL COUNT INCREASED				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
ALLERGIC TRANSFUSION REACTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

ANAPHYLACTIC TRANSFUSION REACTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
INFUSION RELATED REACTION				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
OVERDOSE				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
TOXICITY TO VARIOUS AGENTS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
TRANSFUSION REACTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
TRAUMATIC FRACTURE				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
VASCULAR ACCESS COMPLICATION				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
CARDIAC FAILURE				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

CARDIAC ARREST				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
LEFT VENTRICULAR DYSFUNCTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PERICARDIAL EFFUSION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
TACHYCARDIA				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
SINUS TACHYCARDIA				
subjects affected / exposed	3 / 106 (2.83%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
CEREBRAL ISCHAEMIA				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CEREBROVASCULAR ACCIDENT				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
DEPRESSED LEVEL OF CONSCIOUSNESS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

DYSARTHRIA			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ENCEPHALOPATHY			
subjects affected / exposed	2 / 106 (1.89%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
FACIAL PARESIS			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
HAEMORRHAGE INTRACRANIAL			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HEADACHE			
subjects affected / exposed	8 / 106 (7.55%)		
occurrences causally related to treatment / all	1 / 8		
deaths causally related to treatment / all	0 / 0		
HEMIPARESIS			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LEUKOENCEPHALOPATHY			
subjects affected / exposed	2 / 106 (1.89%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
PARAESTHESIA			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PERIPHERAL MOTOR NEUROPATHY			

subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
PERIPHERAL SENSORY NEUROPATHY				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME				
subjects affected / exposed	4 / 106 (3.77%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
PRESYNCOPE				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SEIZURE				
subjects affected / exposed	5 / 106 (4.72%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
ANAEMIA				
subjects affected / exposed	13 / 106 (12.26%)			
occurrences causally related to treatment / all	12 / 25			
deaths causally related to treatment / all	0 / 0			
FEBRILE NEUTROPENIA				
subjects affected / exposed	81 / 106 (76.42%)			
occurrences causally related to treatment / all	41 / 277			
deaths causally related to treatment / all	0 / 0			
FEBRILE BONE MARROW APLASIA				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
DISSEMINATED INTRAVASCULAR COAGULATION				

subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HAEMORRHAGIC ANAEMIA				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
LEUKOPENIA				
subjects affected / exposed	4 / 106 (3.77%)			
occurrences causally related to treatment / all	6 / 7			
deaths causally related to treatment / all	0 / 0			
LYMPHATIC DISORDER				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PANCYTOPENIA				
subjects affected / exposed	3 / 106 (2.83%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
NEUTROPENIA				
subjects affected / exposed	25 / 106 (23.58%)			
occurrences causally related to treatment / all	18 / 43			
deaths causally related to treatment / all	0 / 0			
THROMBOCYTOPENIA				
subjects affected / exposed	10 / 106 (9.43%)			
occurrences causally related to treatment / all	11 / 19			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
HYPOACUSIS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Eye disorders				

PHOTOPHOBIA				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
VISION BLURRED				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
ABDOMINAL PAIN LOWER				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ABDOMINAL PAIN				
subjects affected / exposed	11 / 106 (10.38%)			
occurrences causally related to treatment / all	2 / 15			
deaths causally related to treatment / all	0 / 0			
ASCITES				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
ANAL HAEMORRHAGE				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
CONSTIPATION				
subjects affected / exposed	3 / 106 (2.83%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
COLITIS				
subjects affected / exposed	10 / 106 (9.43%)			
occurrences causally related to treatment / all	5 / 12			
deaths causally related to treatment / all	0 / 0			
DIARRHOEA				

subjects affected / exposed	21 / 106 (19.81%)			
occurrences causally related to treatment / all	7 / 33			
deaths causally related to treatment / all	0 / 0			
DIARRHOEA HAEMORRHAGIC				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ENTERITIS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
ENTEROCOLITIS				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
GASTRIC HAEMORRHAGE				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
GASTRIC PERFORATION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
GASTRITIS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
GASTROINTESTINAL HAEMORRHAGE				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
GASTROINTESTINAL NECROSIS				

subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HAEMATOCHEZIA				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ILEUS				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
INTESTINAL PERFORATION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
LARGE INTESTINAL ULCER				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
LOWER GASTROINTESTINAL HAEMORRHAGE				
subjects affected / exposed	4 / 106 (3.77%)			
occurrences causally related to treatment / all	3 / 5			
deaths causally related to treatment / all	0 / 0			
NAUSEA				
subjects affected / exposed	6 / 106 (5.66%)			
occurrences causally related to treatment / all	2 / 7			
deaths causally related to treatment / all	0 / 0			
NEUTROPENIC COLITIS				
subjects affected / exposed	7 / 106 (6.60%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
OESOPHAGITIS				

subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PANCREATITIS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PANCREATITIS ACUTE				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
PROCTALGIA				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PROCTITIS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
RECTAL HAEMORRHAGE				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
STOMATITIS				
subjects affected / exposed	15 / 106 (14.15%)			
occurrences causally related to treatment / all	0 / 18			
deaths causally related to treatment / all	0 / 0			
UPPER GASTROINTESTINAL HAEMORRHAGE				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
VOMITING				

subjects affected / exposed	16 / 106 (15.09%)		
occurrences causally related to treatment / all	3 / 22		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HEPATITIS TOXIC			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
VENOOCCLUSIVE LIVER DISEASE			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
DERMATITIS ACNEIFORM			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RASH			
subjects affected / exposed	3 / 106 (2.83%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
RASH GENERALISED			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RASH MACULAR			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RASH MACULO-PAPULAR			

subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SKIN ULCER				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
ACUTE KIDNEY INJURY				
subjects affected / exposed	10 / 106 (9.43%)			
occurrences causally related to treatment / all	1 / 11			
deaths causally related to treatment / all	0 / 0			
BLADDER SPASM				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CYSTITIS NONINFECTIVE				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HAEMATURIA				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
NEPHROLITHIASIS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
URINARY RETENTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
URINARY TRACT OBSTRUCTION				

subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
ADRENAL INSUFFICIENCY			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	2 / 106 (1.89%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
BONE PAIN			
subjects affected / exposed	2 / 106 (1.89%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
MUSCULAR WEAKNESS			
subjects affected / exposed	3 / 106 (2.83%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	2 / 106 (1.89%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
MUSCULOSKELETAL PAIN			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MYALGIA			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

OSTEONECROSIS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PAIN IN EXTREMITY				
subjects affected / exposed	5 / 106 (4.72%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
PAIN IN JAW				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
RHABDOMYOLYSIS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
ABDOMINAL INFECTION				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
BACTERIAL SEPSIS				
subjects affected / exposed	3 / 106 (2.83%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
BACTERAEMIA				
subjects affected / exposed	14 / 106 (13.21%)			
occurrences causally related to treatment / all	0 / 21			
deaths causally related to treatment / all	0 / 0			
BRONCHITIS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CANDIDA INFECTION				

subjects affected / exposed	3 / 106 (2.83%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
CANDIDA PNEUMONIA				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CATHETER SITE INFECTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CELLULITIS				
subjects affected / exposed	3 / 106 (2.83%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
CELLULITIS OF MALE EXTERNAL GENITAL ORGAN				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CLOSTRIDIAL INFECTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CLOSTRIDIUM DIFFICILE COLITIS				
subjects affected / exposed	6 / 106 (5.66%)			
occurrences causally related to treatment / all	2 / 7			
deaths causally related to treatment / all	0 / 0			
CLOSTRIDIUM DIFFICILE INFECTION				
subjects affected / exposed	7 / 106 (6.60%)			
occurrences causally related to treatment / all	0 / 9			
deaths causally related to treatment / all	0 / 0			
COCCIDIOIDOMYCOSIS				

subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CONJUNCTIVITIS				
subjects affected / exposed	3 / 106 (2.83%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
DEVICE RELATED INFECTION				
subjects affected / exposed	14 / 106 (13.21%)			
occurrences causally related to treatment / all	1 / 16			
deaths causally related to treatment / all	0 / 0			
CYTOMEGALOVIRUS INFECTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
EMPYEMA				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ENTEROCOLITIS BACTERIAL				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
ENTEROCOLITIS INFECTIOUS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
ESCHERICHIA BACTERAEMIA				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
ESCHERICHIA SEPSIS				

subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
ESCHERICHIA URINARY TRACT INFECTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
FUNGAL SEPSIS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
GASTROENTERITIS				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
HEPATIC INFECTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HERPES ZOSTER				
subjects affected / exposed	3 / 106 (2.83%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
INFECTION				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
INFLUENZA				
subjects affected / exposed	3 / 106 (2.83%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
KIDNEY INFECTION				

subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
KLEBSIELLA BACTERAEMIA				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
LOCALISED INFECTION				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
LOWER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
LUNG INFECTION				
subjects affected / exposed	10 / 106 (9.43%)			
occurrences causally related to treatment / all	1 / 13			
deaths causally related to treatment / all	0 / 1			
MUCOSAL INFECTION				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
NAIL BED INFECTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
NAIL INFECTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
NEUTROPENIC INFECTION				

subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
OSTEOMYELITIS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
OTITIS MEDIA				
subjects affected / exposed	5 / 106 (4.72%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	0 / 0			
PASTEURELLA INFECTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PELVIC INFECTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PERINEAL CELLULITIS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PERIORBITAL CELLULITIS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PERITONITIS				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
PHARYNGITIS				

subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA				
subjects affected / exposed	10 / 106 (9.43%)			
occurrences causally related to treatment / all	1 / 11			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA BACTERIAL				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA VIRAL				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
POSTOPERATIVE WOUND INFECTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PSEUDOMONAL BACTERAEMIA				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
RASH PUSTULAR				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
RESPIRATORY SYNCYTIAL VIRUS INFECTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SEPSIS				

subjects affected / exposed	20 / 106 (18.87%)			
occurrences causally related to treatment / all	7 / 31			
deaths causally related to treatment / all	0 / 1			
SEPTIC EMBOLUS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SEPTIC SHOCK				
subjects affected / exposed	6 / 106 (5.66%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 0			
SINUSITIS				
subjects affected / exposed	3 / 106 (2.83%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
SKIN INFECTION				
subjects affected / exposed	4 / 106 (3.77%)			
occurrences causally related to treatment / all	2 / 9			
deaths causally related to treatment / all	0 / 0			
SPLENIC INFECTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
STREPTOCOCCAL SEPSIS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SYSTEMIC CANDIDA				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SYSTEMIC MYCOSIS				

subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
TOOTH ABSCESS				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
TOOTH INFECTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
UPPER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
URINARY TRACT INFECTION				
subjects affected / exposed	3 / 106 (2.83%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
URINARY TRACT INFECTION ENTEROCOCCAL				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
VIRAL DIARRHOEA				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
VIRAL UPPER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				

DECREASED APPETITE			
subjects affected / exposed	3 / 106 (2.83%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
DEHYDRATION			
subjects affected / exposed	11 / 106 (10.38%)		
occurrences causally related to treatment / all	3 / 17		
deaths causally related to treatment / all	0 / 0		
HYPERGLYCAEMIA			
subjects affected / exposed	2 / 106 (1.89%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
HYPERKALAEMIA			
subjects affected / exposed	2 / 106 (1.89%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
HYPERNATRAEMIA			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HYPOALBUMINAEMIA			
subjects affected / exposed	3 / 106 (2.83%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
HYPOKALAEMIA			
subjects affected / exposed	9 / 106 (8.49%)		
occurrences causally related to treatment / all	2 / 10		
deaths causally related to treatment / all	0 / 0		
HYPONATRAEMIA			

subjects affected / exposed	8 / 106 (7.55%)		
occurrences causally related to treatment / all	2 / 10		
deaths causally related to treatment / all	0 / 0		
HYPOPHOSPHATAEMIA			
subjects affected / exposed	2 / 106 (1.89%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	DASATINIB		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	106 / 106 (100.00%)		
Vascular disorders			
FLUSHING			
subjects affected / exposed	10 / 106 (9.43%)		
occurrences (all)	13		
HAEMATOMA			
subjects affected / exposed	6 / 106 (5.66%)		
occurrences (all)	8		
HYPERTENSION			
subjects affected / exposed	41 / 106 (38.68%)		
occurrences (all)	93		
HYPOTENSION			
subjects affected / exposed	28 / 106 (26.42%)		
occurrences (all)	55		
PALLOR			
subjects affected / exposed	11 / 106 (10.38%)		
occurrences (all)	19		
General disorders and administration site conditions			
CATHETER SITE ERYTHEMA			
subjects affected / exposed	6 / 106 (5.66%)		
occurrences (all)	7		
ASTHENIA			

subjects affected / exposed	11 / 106 (10.38%)		
occurrences (all)	19		
CATHETER SITE PAIN			
subjects affected / exposed	14 / 106 (13.21%)		
occurrences (all)	18		
CHILLS			
subjects affected / exposed	20 / 106 (18.87%)		
occurrences (all)	37		
FACE OEDEMA			
subjects affected / exposed	8 / 106 (7.55%)		
occurrences (all)	11		
FATIGUE			
subjects affected / exposed	58 / 106 (54.72%)		
occurrences (all)	151		
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	6 / 106 (5.66%)		
occurrences (all)	7		
GAIT DISTURBANCE			
subjects affected / exposed	10 / 106 (9.43%)		
occurrences (all)	16		
MALAISE			
subjects affected / exposed	7 / 106 (6.60%)		
occurrences (all)	8		
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	18 / 106 (16.98%)		
occurrences (all)	30		
MUCOSAL INFLAMMATION			
subjects affected / exposed	51 / 106 (48.11%)		
occurrences (all)	88		
OEDEMA PERIPHERAL			
subjects affected / exposed	17 / 106 (16.04%)		
occurrences (all)	32		
OEDEMA			
subjects affected / exposed	10 / 106 (9.43%)		
occurrences (all)	11		
PAIN			

subjects affected / exposed	28 / 106 (26.42%)		
occurrences (all)	46		
PYREXIA			
subjects affected / exposed	79 / 106 (74.53%)		
occurrences (all)	356		
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	17 / 106 (16.04%)		
occurrences (all)	21		
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	78 / 106 (73.58%)		
occurrences (all)	249		
ATELECTASIS			
subjects affected / exposed	8 / 106 (7.55%)		
occurrences (all)	9		
DYSPNOEA			
subjects affected / exposed	18 / 106 (16.98%)		
occurrences (all)	26		
EPISTAXIS			
subjects affected / exposed	27 / 106 (25.47%)		
occurrences (all)	48		
HYPOXIA			
subjects affected / exposed	15 / 106 (14.15%)		
occurrences (all)	22		
NASAL CONGESTION			
subjects affected / exposed	28 / 106 (26.42%)		
occurrences (all)	52		
OROPHARYNGEAL PAIN			
subjects affected / exposed	35 / 106 (33.02%)		
occurrences (all)	67		
PRODUCTIVE COUGH			
subjects affected / exposed	8 / 106 (7.55%)		
occurrences (all)	13		
PLEURAL EFFUSION			

subjects affected / exposed	16 / 106 (15.09%)		
occurrences (all)	18		
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	10 / 106 (9.43%)		
occurrences (all)	16		
RHINITIS ALLERGIC			
subjects affected / exposed	8 / 106 (7.55%)		
occurrences (all)	9		
RHINORRHOEA			
subjects affected / exposed	37 / 106 (34.91%)		
occurrences (all)	76		
TACHYPNOEA			
subjects affected / exposed	11 / 106 (10.38%)		
occurrences (all)	14		
SNEEZING			
subjects affected / exposed	7 / 106 (6.60%)		
occurrences (all)	7		
WHEEZING			
subjects affected / exposed	13 / 106 (12.26%)		
occurrences (all)	16		
Psychiatric disorders			
AGITATION			
subjects affected / exposed	10 / 106 (9.43%)		
occurrences (all)	20		
ANXIETY			
subjects affected / exposed	15 / 106 (14.15%)		
occurrences (all)	29		
DEPRESSION			
subjects affected / exposed	16 / 106 (15.09%)		
occurrences (all)	20		
INSOMNIA			
subjects affected / exposed	16 / 106 (15.09%)		
occurrences (all)	21		
IRRITABILITY			
subjects affected / exposed	12 / 106 (11.32%)		
occurrences (all)	16		

Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	42 / 106 (39.62%)		
occurrences (all)	186		
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	35 / 106 (33.02%)		
occurrences (all)	102		
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	12 / 106 (11.32%)		
occurrences (all)	23		
BLOOD CREATININE INCREASED			
subjects affected / exposed	9 / 106 (8.49%)		
occurrences (all)	16		
CARDIAC MURMUR			
subjects affected / exposed	12 / 106 (11.32%)		
occurrences (all)	27		
ELECTROCARDIOGRAM QT PROLONGED			
subjects affected / exposed	6 / 106 (5.66%)		
occurrences (all)	18		
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	7 / 106 (6.60%)		
occurrences (all)	15		
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	8 / 106 (7.55%)		
occurrences (all)	126		
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	41 / 106 (38.68%)		
occurrences (all)	316		
PLATELET COUNT DECREASED			
subjects affected / exposed	39 / 106 (36.79%)		
occurrences (all)	368		
WEIGHT DECREASED			
subjects affected / exposed	26 / 106 (24.53%)		
occurrences (all)	38		

WEIGHT INCREASED			
subjects affected / exposed	11 / 106 (10.38%)		
occurrences (all)	36		
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	21 / 106 (19.81%)		
occurrences (all)	192		
Injury, poisoning and procedural complications			
ALLERGIC TRANSFUSION REACTION			
subjects affected / exposed	13 / 106 (12.26%)		
occurrences (all)	18		
ARTHROPOD BITE			
subjects affected / exposed	6 / 106 (5.66%)		
occurrences (all)	8		
CONTUSION			
subjects affected / exposed	32 / 106 (30.19%)		
occurrences (all)	59		
SKIN ABRASION			
subjects affected / exposed	8 / 106 (7.55%)		
occurrences (all)	16		
SUNBURN			
subjects affected / exposed	7 / 106 (6.60%)		
occurrences (all)	7		
TRANSFUSION REACTION			
subjects affected / exposed	6 / 106 (5.66%)		
occurrences (all)	10		
Cardiac disorders			
PERICARDIAL EFFUSION			
subjects affected / exposed	6 / 106 (5.66%)		
occurrences (all)	6		
SINUS TACHYCARDIA			
subjects affected / exposed	19 / 106 (17.92%)		
occurrences (all)	31		
TACHYCARDIA			
subjects affected / exposed	35 / 106 (33.02%)		
occurrences (all)	82		
Nervous system disorders			

DIZZINESS			
subjects affected / exposed	14 / 106 (13.21%)		
occurrences (all)	30		
HEADACHE			
subjects affected / exposed	70 / 106 (66.04%)		
occurrences (all)	246		
LETHARGY			
subjects affected / exposed	7 / 106 (6.60%)		
occurrences (all)	13		
NEUROPATHY PERIPHERAL			
subjects affected / exposed	6 / 106 (5.66%)		
occurrences (all)	12		
PERIPHERAL MOTOR NEUROPATHY			
subjects affected / exposed	12 / 106 (11.32%)		
occurrences (all)	17		
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	13 / 106 (12.26%)		
occurrences (all)	15		
TREMOR			
subjects affected / exposed	8 / 106 (7.55%)		
occurrences (all)	8		
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	83 / 106 (78.30%)		
occurrences (all)	773		
FEBRILE NEUTROPENIA			
subjects affected / exposed	37 / 106 (34.91%)		
occurrences (all)	62		
LEUKOPENIA			
subjects affected / exposed	12 / 106 (11.32%)		
occurrences (all)	46		
NEUTROPENIA			
subjects affected / exposed	43 / 106 (40.57%)		
occurrences (all)	181		
THROMBOCYTOPENIA			

subjects affected / exposed	50 / 106 (47.17%)		
occurrences (all)	385		
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	25 / 106 (23.58%)		
occurrences (all)	44		
Eye disorders			
EYE PAIN			
subjects affected / exposed	8 / 106 (7.55%)		
occurrences (all)	10		
OCULAR HYPERAEMIA			
subjects affected / exposed	7 / 106 (6.60%)		
occurrences (all)	8		
PERIORBITAL OEDEMA			
subjects affected / exposed	9 / 106 (8.49%)		
occurrences (all)	12		
VISION BLURRED			
subjects affected / exposed	15 / 106 (14.15%)		
occurrences (all)	18		
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	11 / 106 (10.38%)		
occurrences (all)	17		
ABDOMINAL PAIN			
subjects affected / exposed	73 / 106 (68.87%)		
occurrences (all)	238		
ABDOMINAL PAIN UPPER			
subjects affected / exposed	19 / 106 (17.92%)		
occurrences (all)	35		
ANAL INFLAMMATION			
subjects affected / exposed	7 / 106 (6.60%)		
occurrences (all)	9		
COLITIS			
subjects affected / exposed	13 / 106 (12.26%)		
occurrences (all)	19		
CONSTIPATION			

subjects affected / exposed	58 / 106 (54.72%)		
occurrences (all)	131		
DIARRHOEA			
subjects affected / exposed	75 / 106 (70.75%)		
occurrences (all)	247		
DYSPEPSIA			
subjects affected / exposed	7 / 106 (6.60%)		
occurrences (all)	11		
HAEMATOCHEZIA			
subjects affected / exposed	14 / 106 (13.21%)		
occurrences (all)	28		
MOUTH ULCERATION			
subjects affected / exposed	8 / 106 (7.55%)		
occurrences (all)	10		
NAUSEA			
subjects affected / exposed	81 / 106 (76.42%)		
occurrences (all)	325		
ORAL PAIN			
subjects affected / exposed	27 / 106 (25.47%)		
occurrences (all)	44		
PROCTALGIA			
subjects affected / exposed	15 / 106 (14.15%)		
occurrences (all)	21		
STOMATITIS			
subjects affected / exposed	49 / 106 (46.23%)		
occurrences (all)	121		
TOOTHACHE			
subjects affected / exposed	9 / 106 (8.49%)		
occurrences (all)	13		
VOMITING			
subjects affected / exposed	83 / 106 (78.30%)		
occurrences (all)	436		
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	21 / 106 (19.81%)		
occurrences (all)	25		

DERMATITIS ACNEIFORM				
subjects affected / exposed	9 / 106 (8.49%)			
occurrences (all)	14			
DRY SKIN				
subjects affected / exposed	19 / 106 (17.92%)			
occurrences (all)	26			
ECCHYMOSIS				
subjects affected / exposed	7 / 106 (6.60%)			
occurrences (all)	15			
ERYTHEMA				
subjects affected / exposed	22 / 106 (20.75%)			
occurrences (all)	36			
PETECHIAE				
subjects affected / exposed	17 / 106 (16.04%)			
occurrences (all)	28			
PAIN OF SKIN				
subjects affected / exposed	6 / 106 (5.66%)			
occurrences (all)	6			
PRURITUS				
subjects affected / exposed	27 / 106 (25.47%)			
occurrences (all)	39			
RASH MACULO-PAPULAR				
subjects affected / exposed	21 / 106 (19.81%)			
occurrences (all)	41			
RASH				
subjects affected / exposed	48 / 106 (45.28%)			
occurrences (all)	120			
SWELLING FACE				
subjects affected / exposed	9 / 106 (8.49%)			
occurrences (all)	9			
RASH PAPULAR				
subjects affected / exposed	8 / 106 (7.55%)			
occurrences (all)	8			
URTICARIA				
subjects affected / exposed	9 / 106 (8.49%)			
occurrences (all)	11			

Renal and urinary disorders			
DYSURIA			
subjects affected / exposed	12 / 106 (11.32%)		
occurrences (all)	16		
HAEMATURIA			
subjects affected / exposed	13 / 106 (12.26%)		
occurrences (all)	17		
URINARY RETENTION			
subjects affected / exposed	6 / 106 (5.66%)		
occurrences (all)	9		
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	48 / 106 (45.28%)		
occurrences (all)	122		
ARTHRALGIA			
subjects affected / exposed	38 / 106 (35.85%)		
occurrences (all)	103		
BONE PAIN			
subjects affected / exposed	22 / 106 (20.75%)		
occurrences (all)	40		
MUSCULAR WEAKNESS			
subjects affected / exposed	21 / 106 (19.81%)		
occurrences (all)	30		
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	8 / 106 (7.55%)		
occurrences (all)	15		
MYALGIA			
subjects affected / exposed	15 / 106 (14.15%)		
occurrences (all)	30		
MUSCULOSKELETAL PAIN			
subjects affected / exposed	15 / 106 (14.15%)		
occurrences (all)	20		
NECK PAIN			
subjects affected / exposed	9 / 106 (8.49%)		
occurrences (all)	15		
OSTEONECROSIS			

subjects affected / exposed	7 / 106 (6.60%)		
occurrences (all)	8		
PAIN IN EXTREMITY			
subjects affected / exposed	62 / 106 (58.49%)		
occurrences (all)	191		
PAIN IN JAW			
subjects affected / exposed	18 / 106 (16.98%)		
occurrences (all)	30		
Infections and infestations			
CANDIDA INFECTION			
subjects affected / exposed	11 / 106 (10.38%)		
occurrences (all)	19		
CELLULITIS			
subjects affected / exposed	10 / 106 (9.43%)		
occurrences (all)	10		
CLOSTRIDIUM DIFFICILE COLITIS			
subjects affected / exposed	11 / 106 (10.38%)		
occurrences (all)	13		
CONJUNCTIVITIS			
subjects affected / exposed	12 / 106 (11.32%)		
occurrences (all)	15		
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	8 / 106 (7.55%)		
occurrences (all)	9		
EAR INFECTION			
subjects affected / exposed	7 / 106 (6.60%)		
occurrences (all)	7		
DEVICE RELATED INFECTION			
subjects affected / exposed	7 / 106 (6.60%)		
occurrences (all)	9		
ENTEROCOLITIS INFECTIOUS			
subjects affected / exposed	10 / 106 (9.43%)		
occurrences (all)	12		
INFLUENZA			
subjects affected / exposed	7 / 106 (6.60%)		
occurrences (all)	7		

LUNG INFECTION				
subjects affected / exposed	8 / 106 (7.55%)			
occurrences (all)	8			
ORAL CANDIDIASIS				
subjects affected / exposed	14 / 106 (13.21%)			
occurrences (all)	23			
PHARYNGITIS				
subjects affected / exposed	10 / 106 (9.43%)			
occurrences (all)	11			
OTITIS MEDIA				
subjects affected / exposed	11 / 106 (10.38%)			
occurrences (all)	15			
PNEUMONIA				
subjects affected / exposed	6 / 106 (5.66%)			
occurrences (all)	6			
RHINITIS				
subjects affected / exposed	10 / 106 (9.43%)			
occurrences (all)	17			
RHINOVIRUS INFECTION				
subjects affected / exposed	7 / 106 (6.60%)			
occurrences (all)	7			
SEPSIS				
subjects affected / exposed	7 / 106 (6.60%)			
occurrences (all)	8			
SINUSITIS				
subjects affected / exposed	18 / 106 (16.98%)			
occurrences (all)	26			
SKIN INFECTION				
subjects affected / exposed	12 / 106 (11.32%)			
occurrences (all)	15			
UPPER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	39 / 106 (36.79%)			
occurrences (all)	60			
URINARY TRACT INFECTION				

subjects affected / exposed	14 / 106 (13.21%)		
occurrences (all)	17		
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	9 / 106 (8.49%)		
occurrences (all)	11		
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	40 / 106 (37.74%)		
occurrences (all)	100		
DEHYDRATION			
subjects affected / exposed	14 / 106 (13.21%)		
occurrences (all)	18		
HYPERGLYCAEMIA			
subjects affected / exposed	23 / 106 (21.70%)		
occurrences (all)	34		
HYPOCALCAEMIA			
subjects affected / exposed	30 / 106 (28.30%)		
occurrences (all)	66		
HYPOALBUMINAEMIA			
subjects affected / exposed	34 / 106 (32.08%)		
occurrences (all)	54		
HYPOKALAEMIA			
subjects affected / exposed	50 / 106 (47.17%)		
occurrences (all)	175		
HYPOMAGNESAEMIA			
subjects affected / exposed	19 / 106 (17.92%)		
occurrences (all)	36		
HYPONATRAEMIA			
subjects affected / exposed	23 / 106 (21.70%)		
occurrences (all)	41		
HYPOPHOSPHATAEMIA			
subjects affected / exposed	23 / 106 (21.70%)		
occurrences (all)	43		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 September 2011	The following amendment was developed to incorporate two key changes including: 1) Changing the statistical design of the trial to allow comparison to historical external controls. Specifically, the 3-year event free survival (EFS) of dasatinib plus chemotherapy will be compared to the 3-year EFS of chemotherapy alone from the Associazione Italiana di Ematologia Pediatrica - Berlin-Frankfurt-Muenster ALL 2000 (AIEOP BFM 2000) trial and the 3-year EFS of imatinib plus chemotherapy from the European intergroup Study on post induction treatment of Philadelphia positive Acute Lymphoblastic Leukemia (EsPhALL). This analysis will improve the ability to interpret the safety and efficacy of dasatinib added to chemotherapy among other treatment options for this pediatric leukemia. 2) Incorporating additional supportive care options for chemotherapy to accommodate the standard of care at sites in the United Kingdom (UK). Additionally, typographical errors were also corrected.
07 December 2012	The key purposes of this amendment are to incorporate the following key changes: 1) Introduce a new pediatric formulation of dasatinib. 2) Address lack of availability of native-asparaginase in the United States and allow use of Peg-Asparaginase upfront in such instances as well as provide more detailed instruction for dose modifications of the various asparaginase formulations. 3) Indicate that the BCR-ABL mutation status will be reported for baseline and at time of progression as a secondary objective instead of as an exploratory objective. 4) Allow Philadelphia chromosome positivity from peripheral blood to be acceptable for study entry. 5) Expand the window for screening activities to 21 days. 6) Modify the definition of high risk group and low/standard risk group in response to Induction 1A treatment. 7) Provides for clarifications, fixes inconsistencies across sections of the protocol and corrects various typographical errors.
31 July 2013	The key purposes of this amendment are to incorporate the following key changes: 1) Increase the number of treated subjects from 75 to at least 75 and up to 90. 2) Modify language regarding pregnancy prevention. 3) Incorporate recommendations for subject management and supportive care during High Risk (HR) Blocks 1-3. 4) Provides for clarifications, fixes inconsistencies across sections of the protocol and corrects various typographical errors.
28 October 2013	The key purposes of this amendment are to incorporate the following changes: 1) Add mandatory supportive care measures during the 3 High Risk Blocks 2) Provide updates to the WOCBP language to harmonize this language with the current BMS directives for WOCBP.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported