Clinical trial results:
A Phase 1/2 Study of Bosutinib (SKI-606) in Philadelphia Chromosome Positive Leukemias

Summary

EudraCT number	2005-004230-40
Trial protocol	DE ES HU AT FI SE GB
Global end of trial date	06 August 2015

Results information

Result version number	v1 (current)
This version publication date	20 August 2016
First version publication date	20 August 2016

Trial information

Trial identification

Sponsor protocol code	3160A4-200-WW

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00261846
WHO universal trial number (UTN)	-
Other trial identifiers	Alias ID: B1871006

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 August 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 August 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This open-label, multicentre, continuous dosing, 2-part safety and efficacy Phase 1/2 study of oral bosutinib once daily in participants with Philadelphia chromosome-positive (Ph+) leukemia primarily defined the maximum tolerated dose (MTD) in participants with chronic phase (CP) chronic myelogenous leukemia (CML) resistant or refractory to imatinib and evaluated the overall pharmacokinetic (PK) parameters in this population. Secondary objectives were to determine the rate of major cytogenetic response (MCyR) in CP CML participants and to obtain data on the ability of bosutinib to inhibit phosphorylation of Crk-like protein (CrkL) and breakpoint cluster region-abelson kinase (Bcr-Abl) at various dose levels of bosutinib.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Council for Harmonisation Good Clinical Practice Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial participants. The final protocol, amendments, and informed consent documentation were reviewed and approved by the Institutional Review Board(s) and/or Independent Ethics Committee(s) at each of the investigational centers participating in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 January 2006
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 20
Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Brazil: 26
Country: Number of subjects enrolled	Canada: 16
Country: Number of subjects enrolled	Chile: 2
Country: Number of subjects enrolled	China: 43
Country: Number of subjects enrolled	Colombia: 4
Country: Number of subjects enrolled	Germany: 40
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	Finland: 7

Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Hong Kong: 6
Country: Number of subjects enrolled	Hungary: 10
Country: Number of subjects enrolled	India: 22
Country: Number of subjects enrolled	Italy: 53
Country: Number of subjects enrolled	Korea, Republic of: 32
Country: Number of subjects enrolled	Mexico: 4
Country: Number of subjects enrolled	Netherlands: 17
Country: Number of subjects enrolled	Norway: 3
Country: Number of subjects enrolled	Peru: 6
Country: Number of subjects enrolled	Russian Federation: 66
Country: Number of subjects enrolled	Singapore: 5
Country: Number of subjects enrolled	South Africa: 9
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	United States: 146
Worldwide total number of subjects	570
EEA total number of subjects	152

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)	451
From 65 to 84 years	117
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were analyzed based on worst disease stage since diagnosis and previous tyrosine kinase inhibitor usage prior to screening and classified into 1 of 11 cohorts.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Bosutinib 400 mg (Part 1)

Arm description:

Single oral dose of bosutinib 400 milligram (mg) on Day 1 and then bosutinib 400 mg orally once daily continuously from Day 3 up to Week 4. All participants who completed treatment in Part 1 were continued in chronic phase second-line chronic myelogenous leukemia (CP2L-CML) Part 2 of the study.

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

Dosage and administration details:

Bosutinib 400 mg administered orally once daily with water and food to potentially improve tolerance and absorption.

Arm title	Bosutinib 500 mg (Part 1)

Arm description:

Single oral dose of bosutinib 500 mg on Day 1 and then bosutinib 500 mg orally once daily continuously from Day 3 up to Week 4. All participants who completed treatment in Part 1 were continued in chronic phase second-line chronic myelogenous leukemia (CP2L-CML) Part 2 of the study.

Arm type	Experimental
Investigational medicinal product name	Bosutinib
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Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Bosutinib 500 mg administered orally once daily with water and food to potentially improve tolerance and absorption.

Arm title	Bosutinib 600 mg (Part 1)

Arm description:

Single oral dose of bosutinib 600 mg on Day 1 and then bosutinib 600 mg orally once daily continuously from Day 3 up to Week 4. Eleven participants who completed treatment in Part 1 were continued in chronic phase second-line chronic myelogenous leukemia (CP2L-CML) Part 2 of the study and 1 participant was continued in advanced phase chronic myelogenous leukemia (AP-CML) Part 2 of the study.

Arm type	Experimental

Investigational medicinal product name	Bosutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Bosutinib 600 mg administered orally once daily with water and food to potentially improve tolerance and absorption.

Arm title	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)

Arm description:

Bosutinib 500 mg was administered orally once-daily in participants with chronic phase second-line (CP2L) imatinib (IM) resistant/refractory (R) chronic myelogenous leukemia (CML); who had no prior proto-oncogene tyrosine-protein kinase sarcoma (Src), Abelson kinase (Abl), or Src-Abl inhibitor exposure other than IM.

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

Dosage and administration details:

Bosutinib 500 mg administered orally once daily with water and food to potentially improve tolerance and absorption.

Arm title	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)

Arm description:

Bosutinib 500 mg was administered orally once-daily in participants with chronic phase second-line (CP2L) imatinib (IM) intolerant (I) chronic myelogenous leukemia (CML); who had no prior proto-oncogene tyrosine-protein kinase Src, Abl, or Src-Abl inhibitor exposure other than IM.

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

Dosage and administration details:

Bosutinib 500 mg administered orally once daily with water and food to potentially improve tolerance and absorption.

Arm title	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)

Arm description:

Bosutinib 500 mg was administered orally once-daily in participants with chronic phase third-line (CP3L) imatinib (IM) resistant/intolerant (R/I), dasatinib (D) and nilotinib (NI) resistant/intolerant (R/I) or imatinib (IM) resistant/intolerant (R/I) and nilotinib (NI) intolerant (I) chronic myelogenous leukemia (CML).

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

Dosage and administration details:

Bosutinib 500 mg administered orally once daily with water and food to potentially improve tolerance and absorption.

Arm title	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)

Arm description:

Bosutinib 500 mg was administered orally once-daily in participants with chronic phase third-line (CP3L) imatinib (IM) resistant/intolerant (R/I) and dasatinib (D) resistant (R) chronic myelogenous leukemia (CML).

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

Dosage and administration details:

Bosutinib 500 mg administered orally once daily with water and food to potentially improve tolerance and absorption.

Arm title	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)

Arm description:

Bosutinib 500 mg was administered orally once-daily in participants with chronic phase third-line (CP3L) imatinib (IM) resistant/intolerant (R/I) and dasatinib (D) intolerant (I) chronic myelogenous leukemia (CML).

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

Dosage and administration details:

Bosutinib 500 mg administered orally once daily with water and food to potentially improve tolerance and absorption.

Arm title	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)

Arm description:

Bosutinib 500 mg was administered orally once-daily in participants with chronic phase third-line (CP3L) imatinib (IM) resistant/intolerant (R/I) and nilotinib (NI) resistant (R) chronic myelogenous leukemia (CML).

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

Dosage and administration details:

Bosutinib 500 mg administered orally once daily with water and food to potentially improve tolerance and absorption.

Arm title	AP-CML Total (Part 2)

Arm description:

All participants who received bosutinib 500 mg orally once daily in advanced phase (AP) chronic myelogenous leukemia (CML) who were imatinib (IM) resistant/intolerant (R/I) or Multi-TKI (multiple tyrosine kinase inhibitor: imatinib, dasatinib and/or nilotinib) resistant/intolerant (R/I).

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

Dosage and administration details:

Bosutinib 500 mg administered orally once daily with water and food to potentially improve tolerance

and absorption.

Arm title	BP-CML Total (Part 2)

Arm description:

All participants who received bosutinib 500 mg orally once daily in blast phase (BP) chronic myelogenous leukemia (CML) who were imatinib (IM) resistant/intolerant (R/I) or Multi-TKI (multiple tyrosine kinase inhibitor: imatinib, dasatinib and/or nilotinib) resistant/intolerant (R/I).

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

Dosage and administration details:

Bosutinib 500 mg administered orally once daily with water and food to potentially improve tolerance and absorption.

Arm title	Bosutinib 500 mg, Ph+ ALL (Part 2)

Arm description:

Bosutinib 500 mg was administered orally once-daily in participants with philadelphia chromosome-positive acute lymphocytic leukemia (Ph+ ALL).

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

Dosage and administration details:

Bosutinib 500 mg administered orally once daily with water and food to potentially improve tolerance and absorption.

Number of subjects in period 1	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)
Started	3	3	12
Completed	0	0	0
Not completed	3	3	12
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	-	-	-
Extension study	-	-	-
Discontinuation of study by sponsor	-	-	-
Unspecified	-	-	-
Lost to follow-up	-	-	-
Continued in to Part 2	3	3	12

Number of subjects in period 1	Bosutinib 500 mg, CP2L-CML IM-R	Bosutinib 500 mg, CP2L-CML IM-I (Part	Bosutinib 500 mg, CP3L-CML IM R/I,

	(Part 2)	2)	(D+NI) R/I or NI-I (Part 2)
Started	195	89	5
Completed	60	39	3
Not completed	135	50	2
Adverse event, serious fatal	37	7	1
Consent withdrawn by subject	9	8	1
Extension study	61	27	-
Discontinuation of study by sponsor	1	-	-
Unspecified	15	4	-
Lost to follow-up	12	4	-
Continued in to Part 2	-	-	-

Number of subjects in period 1	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)
Started	38	50	26
Completed	16	21	12
Not completed	22	29	14
Adverse event, serious fatal	10	12	3
Consent withdrawn by subject	3	3	-
Extension study	4	9	5
Discontinuation of study by sponsor	-	-	1
Unspecified	1	5	4
Lost to follow-up	4	-	1
Continued in to Part 2	-	-	-

Number of subjects in period 1	AP-CML Total (Part 2)	BP-CML Total (Part 2)	Bosutinib 500 mg, Ph+ ALL (Part 2)
Started	79	64	24
Completed	30	15	1
Not completed	49	49	23
Adverse event, serious fatal	30	44	22
Consent withdrawn by subject	2	-	-
Extension study	9	1	1
Discontinuation of study by sponsor	-	-	-
Unspecified	4	-	-
Lost to follow-up	4	4	-
Continued in to Part 2	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	570	570	
Age, Customized Units: Participants			
<18 years	0	0	
Between 18 and 64 years	451	451	
Between 65 and 84 years	117	117	
>=85 years	2	2	
Age continuous Units: years			
arithmetic mean	51.6		
full range (min-max)	18 to 91	-	
Gender, Male/Female Units: participants			
Female	270	270	
Male	300	300	

End points

End points reporting groups

Reporting group title	Bosutinib 400 mg (Part 1)
Reporting group description:	
Single oral dose of bosutinib 400 milligram (mg) on Day 1 and then bosutinib 400 mg orally once daily continuously from Day 3 up to Week 4. All participants who completed treatment in Part 1 were continued in chronic phase second-line chronic myelogenous leukemia (CP2L-CML) Part 2 of the study.	
Reporting group title	Bosutinib 500 mg (Part 1)
Reporting group description:	
Single oral dose of bosutinib 500 mg on Day 1 and then bosutinib 500 mg orally once daily continuously from Day 3 up to Week 4. All participants who completed treatment in Part 1 were continued in chronic phase second-line chronic myelogenous leukemia (CP2L-CML) Part 2 of the study.	
Reporting group title	Bosutinib 600 mg (Part 1)
Reporting group description:	
Single oral dose of bosutinib 600 mg on Day 1 and then bosutinib 600 mg orally once daily continuously from Day 3 up to Week 4. Eleven participants who completed treatment in Part 1 were continued in chronic phase second-line chronic myelogenous leukemia (CP2L-CML) Part 2 of the study and 1 participant was continued in advanced phase chronic myelogenous leukemia (AP-CML) Part 2 of the study.	
Reporting group title	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)
Reporting group description:	
Bosutinib 500 mg was administered orally once-daily in participants with chronic phase second-line (CP2L) imatinib (IM) resistant/refractory (R) chronic myelogenous leukemia (CML); who had no prior proto-oncogene tyrosine-protein kinase sarcoma (Src), Abelson kinase (Abl), or Src-Abl inhibitor exposure other than IM.	
Reporting group title	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)
Reporting group description:	
Bosutinib 500 mg was administered orally once-daily in participants with chronic phase second-line (CP2L) imatinib (IM) intolerant (I) chronic myelogenous leukemia (CML); who had no prior proto-oncogene tyrosine-protein kinase Src, Abl, or Src-Abl inhibitor exposure other than IM.	
Reporting group title	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)
Reporting group description:	
Bosutinib 500 mg was administered orally once-daily in participants with chronic phase third-line (CP3L) imatinib (IM) resistant/intolerant (R/I), dasatinib (D) and nilotinib (NI) resistant/intolerant (R/I) or imatinib (IM) resistant/intolerant (R/I) and nilotinib (NI) intolerant (I) chronic myelogenous leukemia (CML).	
Reporting group title	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Reporting group description:	
Bosutinib 500 mg was administered orally once-daily in participants with chronic phase third-line (CP3L) imatinib (IM) resistant/intolerant (R/I) and dasatinib (D) resistant (R) chronic myelogenous leukemia (CML).	
Reporting group title	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)
Reporting group description:	
Bosutinib 500 mg was administered orally once-daily in participants with chronic phase third-line (CP3L) imatinib (IM) resistant/intolerant (R/I) and dasatinib (D) intolerant (I) chronic myelogenous leukemia (CML).	
Reporting group title	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)
Reporting group description:	
Bosutinib 500 mg was administered orally once-daily in participants with chronic phase third-line (CP3L) imatinib (IM) resistant/intolerant (R/I) and nilotinib (NI) resistant (R) chronic myelogenous leukemia (CML).	
Reporting group title	AP-CML Total (Part 2)
Reporting group description:	
All participants who received bosutinib 500 mg orally once daily in advanced phase (AP) chronic myelogenous leukemia (CML) who were imatinib (IM) resistant/intolerant (R/I) or Multi-TKI (multiple tyrosine kinase inhibitor: imatinib, dasatinib and/or nilotinib) resistant/intolerant (R/I).	

Reporting group title	BP-CML Total (Part 2)

Reporting group description:

All participants who received bosutinib 500 mg orally once daily in blast phase (BP) chronic myelogenous leukemia (CML) who were imatinib (IM) resistant/intolerant (R/I) or Multi-TKI (multiple tyrosine kinase inhibitor: imatinib, dasatinib and/or nilotinib) resistant/intolerant (R/I).

Reporting group title	Bosutinib 500 mg, Ph+ ALL (Part 2)

Reporting group description:

Bosutinib 500 mg was administered orally once-daily in participants with philadelphia chromosome-positive acute lymphocytic leukemia (Ph+ ALL).

Subject analysis set title	Bosutinib 500 mg, AP-CML IM R/I (Part 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Bosutinib 500 mg was administered orally once-daily in participants with advanced phase (AP) imatinib (IM) resistant/intolerant (R/I) chronic myelogenous leukemia (CML); who had no prior proto-oncogene tyrosine-protein kinase sarcoma (Src), abelson kinase (Abl), or Src-Abl inhibitor exposure other than IM.

Subject analysis set title	Bosutinib 500 mg, AP-CML Multi-TKI R/I (Part 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Bosutinib 500 mg was administered orally once-daily in participants with advanced phase (AP) Multi-TKI (multiple tyrosine kinase inhibitor: imatinib, dasatinib and/or nilotinib) resistant/intolerant (R/I) chronic myelogenous leukemia (CML).

Subject analysis set title	Bosutinib 500 mg, BP-CML IM R/I (Part 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Bosutinib 500 mg was administered orally once-daily in participants with blast phase (BP) imatinib (IM) resistant/intolerant (R/I) chronic myelogenous leukemia (CML).

Subject analysis set title	Bosutinib 500 mg, BP-CML Multi-TKI R/I (Part 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Bosutinib 500 mg was administered orally once-daily in participants with blast phase (BP) Multi-TKI (multiple tyrosine kinase inhibitor: imatinib, dasatinib and/or nilotinib) resistant/intolerant (R/I) chronic myelogenous leukemia (CML).

Primary: Number of Participants With Dose Limiting Toxicity (DLT)

End point title	Number of Participants With Dose Limiting Toxicity (DLT)[1][2]

End point description:

DLT was defined as any of the following events occurring during the first 28 days of study medication and considered at least possibly-related to study medication: any grade 3 or 4 clinically-relevant non-hematologic toxicity, any clinically-significant grade 2 non-hematologic toxicity that requires 14 days to resolve (to grade 1).
Safety population included all participants who received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

Part 1 Baseline up to Day 28

Notes:

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

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	12	
Units: participants	0	0	1	

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Tolerated Dose (MTD)

End point title	Maximum Tolerated Dose (MTD)[3][4]

End point description:

MTD was defined as highest dose level for which no more than 1 participant in a dose cohort experienced DLT. DLT was defined as any of the following events occurring during the first 28 days of study medication and considered at least possibly-related to study medication: any grade 3 or 4 clinically-relevant non-hematologic toxicity, any clinically-significant grade 2 non-hematologic toxicity that requires 14 days to resolve (to grade 1).9999 = not estimable, MTD was not achieved since no more than 1 DLT was observed in any cohort. At the 600mg dose level, 1 DLT and several treatment related grade 2 toxicities were observed, thus, Bosutinib 500 mg was selected as the recommended dose for part 2.
Safety population, included all participants who received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

Part 1 Baseline up to Day 28

Notes:

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

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	12	
Units: mg	9999	9999	9999	

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Plasma Concentration (Cmax) - Part 1

End point title	Maximum Observed Plasma Concentration (Cmax) - Part 1[5][6]

End point description:

Evaluable population included all enrolled participants who received at least 1 dose of study medication and had an adequate baseline efficacy assessment.

End point type	Primary

End point timeframe:

0 (pre-dose), 1, 2, 3, 4, 6, 8, 24, 48 hours post-dose on Day 1

Notes:

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

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	12	
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)	89.3 (± 50)	101 (± 35.6)	120 (± 40.2)	

Statistical analyses

No statistical analyses for this end point

Primary: Time to Reach Maximum Observed Plasma Concentration (Tmax) - Part 1

End point title	Time to Reach Maximum Observed Plasma Concentration (Tmax) - Part 1[7][8]

End point description:

Evaluable population included all enrolled participants who received at least one dose of study medication and had an adequate baseline efficacy assessment.

End point type	Primary

End point timeframe:

0 (pre-dose), 1, 2, 3, 4, 6, 8, 24, 48 hours post-dose on Day 1

Notes:

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

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	12	
Units: hours (hrs)				
median (full range (min-max))	4 (3.33 to 48.08)	6 (6 to 6)	4 (2.17 to 49.33)	

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Decay Half-Life (t1/2) - Part 1

End point title	Plasma Decay Half-Life (t1/2) - Part 1[9][10]

End point description:

Plasma decay half-life is the time measured for the plasma concentration to decrease by one half.9999 = not estimable, standard deviation was not estimable since only 2 participants were evaluable.
Evaluable population included all enrolled participants who received at least 1 dose of study medication and had an adequate baseline efficacy assessment. 'N' (number of participants analyzed) signifies number of participants who were evaluable for this measure.

End point type	Primary

End point timeframe:

0 (pre-dose), 1, 2, 3, 4, 6, 8, 24, 48 hours post-dose on Day 1

Notes:

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

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3	8	
Units: hrs				
arithmetic mean (standard deviation)	22.91 (± 9999)	22.46 (± 1.73)	22.24 (± 5.03)	

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Curve From Time Zero to Last Quantifiable Concentration [AUC(0-48)] - Part 1

End point title	Area Under the Curve From Time Zero to Last Quantifiable Concentration [AUC(0-48)] - Part 1[11][12]

End point description:

AUC(0-48)= Area under the plasma concentration versus time curve from time zero (pre-dose) to time of last quantifiable concentration (0-48).
Evaluable population included all enrolled participants who received at least 1 dose of study medication and had an adequate baseline efficacy assessment.

End point type	Primary

End point timeframe:

0 (pre-dose), 1, 2, 3, 4, 6, 8, 24, 48 hours post-dose on Day 1

Notes:

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

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	12	
Units: ng*hr/mL				
arithmetic mean (standard deviation)	1850 (± 710)	2060 (± 483)	2340 (± 1140)	

Statistical analyses

No statistical analyses for this end point

Primary: Area under the Concentration-Time Curve (AUC) - Part 1

End point title	Area under the Concentration-Time Curve (AUC) - Part 1[13][14]

End point description:

AUC is a measure of the serum concentration of the drug over time. It is used to characterize drug absorption.
9999 = not estimable, standard deviation was not estimable since only 2 participants were evaluable
Evaluable population included all enrolled participants who received at least 1 dose of study medication and had an adequate baseline efficacy assessment. 'N' (number of participants analyzed) signifies number of participants who were evaluable
for this measure.

End point type	Primary

End point timeframe:

0 (pre-dose), 1, 2, 3, 4, 6, 8, 24, 48 hours post-dose on Day 1

Notes:

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

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3	8	
Units: ng*hr/mL				
arithmetic mean (standard deviation)	2530 (± 9999)	2760 (± 687)	2420 (± 457)	

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Oral Clearance (CL/F) - Part 1

End point title	Apparent Oral Clearance (CL/F) - Part 1[15][16]

End point description:

Clearance of a drug is a measure of the rate at which a drug is metabolized or eliminated by normal biological processes. Clearance obtained after oral dose (apparent oral clearance) is influenced by the fraction of the dose absorbed. Clearance was estimated from population pharmacokinetic (PK) modeling. Drug clearance is a quantitative measure of the rate at which a drug substance is removed from the

blood.
9999 = not estimable.
Evaluable population included all enrolled participants who received at least 1 dose of study medication and had an adequate baseline efficacy assessment. 'N' (number of participants analyzed) signifies number of participants who were evaluable for this measure.

End point type	Primary

End point timeframe:

0 (pre-dose), 1, 2, 3, 4, 6, 8, 24, 48 hours post-dose on Day 1

Notes:

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

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3	8	
Units: liter per hour (L/hr)				
arithmetic mean (standard deviation)	177 (± 9999)	189 (± 47.5)	258 (± 61.2)	

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Volume of Distribution (Vz/F) - Part 1

End point title	Apparent Volume of Distribution (Vz/F) - Part 1[17][18]

End point description:

Volume of distribution is defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired plasma concentration of a drug. Apparent volume of distribution after oral dose (Vz/F) is influenced by the fraction absorbed.
Evaluable population included all enrolled participants who received at least 1 dose of study medication and had an adequate baseline efficacy assessment. 'N' (number of participants analyzed) signifies number of participants who were evaluable
for this measure.

End point type	Primary

End point timeframe:

0 (pre-dose), 1, 2, 3, 4, 6, 8, 24, 48 hours post-dose on Day 1

Notes:

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

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	8	
Units: liter				
arithmetic mean (standard deviation)	6050 (± 3550)	6080 (± 1230)	8540 (± 3820)	

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Plasma Concentration at Steady State (Cmax,ss) - Part 1

End point title	Maximum Observed Plasma Concentration at Steady State (Cmax,ss) - Part 1[19][20]

End point description:

Maximum plasma concentration over 24 hours at steady state (ss), on Day 15.
Evaluable population included all enrolled participants who received at least 1 dose of study medication and had an adequate baseline efficacy assessment. 'N' (number of participants analyzed) signifies number of participants who were evaluable
for this measure.

End point type	Primary

End point timeframe:

0 (pre-dose), 1, 2, 3, 4, 6, 8, 24 hours post-dose on Day 15

Notes:

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

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	10	
Units: ng/mL				
arithmetic mean (standard deviation)	146 (± 20)	200 (± 11.9)	208 (± 73.3)	

Statistical analyses

No statistical analyses for this end point

Primary: Time to Reach Maximum Observed Plasma Concentration at Steady State (Tmax,ss) - Part 1

End point title	Time to Reach Maximum Observed Plasma Concentration at Steady State (Tmax,ss) - Part 1[21][22]

End point description:

Time to reach maximum observed plasma concentration over 24 hours at steady state (ss), on Day 15.
Evaluable population included all enrolled participants who received at least 1 dose of study medication

and had an adequate baseline efficacy assessment.

End point type	Primary

End point timeframe:

0 (pre-dose), 1, 2, 3, 4, 6, 8, 24 hours post-dose on Day 15

Notes:

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

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	12	
Units: hrs				
median (full range (min-max))	4.05 (3.08 to 6.08)	6.05 (4 to 8)	6 (2.83 to 11.08)	

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Decay Half-Life at Steady State (t1/2,ss) - Part 1

End point title	Plasma Decay Half-Life at Steady State (t1/2,ss) - Part 1[23][24]

End point description:

Plasma decay half-life is the time measured for the plasma concentration to decrease by one half. Plasma decay half-life over 24 hours at steady state (ss), on Day 15 was calculated.
Evaluable population included all enrolled participants who received at least 1 dose of study medication and had an adequate baseline efficacy assessment. 'N' (number of participants analyzed) signifies number of participants who were evaluable for this measure.

End point type	Primary

End point timeframe:

0 (pre-dose), 1, 2, 3, 4, 6, 8, 24 hours post-dose on Day 15

Notes:

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

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	7	
Units: hrs				
arithmetic mean (standard deviation)	45.96 (± 32.3)	21.71 (± 4.64)	25.87 (± 24.85)	

Statistical analyses

No statistical analyses for this end point

Primary: Area under the Concentration-Time Curve at Steady State (AUCss) - Part 1

End point title	Area under the Concentration-Time Curve at Steady State (AUCss) - Part 1[25][26]

End point description:

AUC is a measure of the serum concentration of the drug over time. It is used to characterize drug absorption. AUC over 24 hours at steady state (ss), on Day 15 was calculated.
Evaluable population included all enrolled participants who received at least 1 dose of study medication and had an adequate baseline efficacy assessment. 'N' (number of participants analyzed) signifies number of participants who were evaluable for this measure.

End point type	Primary

End point timeframe:

0 (pre-dose), 1, 2, 3, 4, 6, 8, 24 hours post-dose on Day 15

Notes:

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

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	9	
Units: ng*hr/mL				
arithmetic mean (standard deviation)	2720 (± 442)	3650 (± 425)	3630 (± 1270)	

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Oral Clearance at Steady State (CL/F,ss) - Part 1

End point title	Apparent Oral Clearance at Steady State (CL/F,ss) - Part

End point description:

Clearance of a drug is a measure of the rate at which a drug is metabolized or eliminated by normal biological processes. Clearance obtained after oral dose (apparent oral clearance) is influenced by the fraction of the dose absorbed. Clearance was estimated from population pharmacokinetic (PK) modeling. Drug clearance is a quantitative measure of the rate at which a drug substance is removed from the blood. Apparent oral clearance over 24 hours at steady state (ss), on Day 15 was calculated.
Evaluable population included all enrolled participants who received at least 1 dose of study medication and had an adequate baseline efficacy assessment. 'N' (number of participants analyzed) signifies number of participants who were evaluable for this measure.

End point type	Primary

End point timeframe:

0 (pre-dose), 1, 2, 3, 4, 6, 8, 24 hours post-dose on Day 15

Notes:

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

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	9	
Units: L/hr				
arithmetic mean (standard deviation)	150 (± 23.2)	138 (± 16.6)	185 (± 66.2)	

Statistical analyses

No statistical analyses for this end point

Primary: Accumulation Ratio (R)

End point title	Accumulation Ratio (R)[29][30]

End point description:

R=accumulation ratio (AUCss on Day 15/AUC0-24 on Day 1)
Evaluable population included all enrolled participants who received at least 1 dose of study medication and had an adequate baseline efficacy assessment. 'N' (number of participants analyzed) signifies number of participants who were evaluable for this measure.

End point type	Primary

End point timeframe:

0 (pre-dose), 1, 2, 3, 4, 6, 8, 24 hours post-dose on Day 1 and Day 15

Notes:

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

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	9	
Units: ratio				
arithmetic mean (standard deviation)	3.1 (± 1.4)	2.8 (± 0.8)	2.5 (± 0.9)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With MCyR at Week 24 in Chronic Phase Second-line Imatinib Resistant CML Population - Part 2

End point title	Percentage of Participants With MCyR at Week 24 in Chronic Phase Second-line Imatinib Resistant CML Population - Part 2[31][32]

End point description:

CyR is based on the prevalence of Ph+ cells. Major cytogenetic response was categorized as either CCyR or partial CyR (PCyR). CCyR was achieved when there was 0 percent (%) Ph+ cells from at least 20 metaphases from conventional bone marrow cytogenetics or less than (<) 1% positive cells from at least 200 cells analyzed from fluorescent in situ hybridization (FISH). PCyR was achieved when 1 to 35% Ph+ cells were present.
Cytogenetic evaluable population included all enrolled participants who received at least one dose of study medication and had an adequate baseline cytogenetic assessment.

End point type	Primary

End point timeframe:

Week 24

Notes:

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

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)			
Subject group type	Reporting group			
Number of subjects analysed	182			
Units: percentage of participants				
number (confidence interval 95%)	35.7 (28.8 to 43.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Major Cytogenetic Response (MCyR) - Part 1

End point title	Percentage of Participants With Major Cytogenetic Response (MCyR) - Part 1[33]

End point description:

Cytogenetic response (CyR) is based on the prevalence of Philadelphia positive (Ph+) cells. Major cytogenetic response was categorized as either complete cytogenetic response (CCyR) or partial cytogenetic response (PCyR). CCyR was achieved when there was 0% Ph+ cells from at least 20 metaphases from conventional bone marrow cytogenetics or <1% positive cells from at least 200 cells analyzed from FISH. PCyR was achieved when 1 to 35% Ph+ cells were present.
Cytogenetic evaluable population included all enrolled participants who received at least 1 dose of study medication and had an adequate baseline cytogenetic assessment.

End point type	Secondary

End point timeframe:

Week 12, thereafter assessed every 12 weeks up to 2 years then every 24 weeks thereafter

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	12	
Units: percentage of participants				
number (confidence interval 95%)	66.7 (9.4 to 99.2)	33.3 (0.8 to 90.6)	50 (21.1 to 78.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phosphorylation Inhibition of Breakpoint Cluster Region-Abelson Kinase (bcr-Abl) - Part 1

End point title	Phosphorylation Inhibition of Breakpoint Cluster Region-Abelson Kinase (bcr-Abl) - Part 1[34]

End point description:

bcr-Abl is a protein resulting from the transcription of the Philadelphia chromosome following 9:22 chromosomal translocation, and phosphorylation inhibition of which correlates with inhibition of tumor cell growth.
Data was not summarized since inadequate data included the issue that molecular transcript analyses could not be performed, because of potential sample quality issues due to time required to transport the specimens from the few investigational sites to the central laboratory.

End point type	Secondary

End point timeframe:

Baseline, Week 4, 8, 12, thereafter assessed every 12 weeks up to 2 years then every 24 weeks

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[35]	0[36]	0[37]	
Units: moles per 100 cells (mol/100 cells)				
number (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[35] - Data not summarized, molecular transcript analyses not performed due to poor sample quality.

[36] - Data not summarized, molecular transcript analyses not performed due to poor sample quality.

[37] - Data not summarized, molecular transcript analyses not performed due to poor sample quality.

Statistical analyses

No statistical analyses for this end point

Secondary: Phosphorylation Inhibition of Crk Like (CrkL) Protein at Baseline - Part 1

End point title	Phosphorylation Inhibition of Crk Like (CrkL) Protein at Baseline - Part 1[38]

End point description:

CrkL is a protein, phosphorylation of which has been shown to correlate with CML cell growth; and conversely of their phosphorylation correlates with inhibition of tumor cell growth. Phosphorylation of CrkL was monitored in whole blood cells, as well as in the cluster of differentiation 3 (CD3+) (T cell), CD19+ (B cell) and CD34+ (blast cell) compartments by using fluorescent activated cell sorter (FACS) flow cytometry.
Evaluable population included all enrolled participants who received at least 1 dose of study medication and had an adequate baseline efficacy assessment. 'N' (number of participants analyzed) signifies number of participants who were evaluable for this measure.

End point type	Secondary

End point timeframe:

0 (pre-dose) on Day 1 (Baseline)

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3	10	
Units: mol/100 cells				
arithmetic mean (standard deviation)	457075 (± 559841.9)	297967.33 (± 171643.3)	397795.4 (± 552536.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Phosphorylation Inhibition of Crk Like Protein (CrkL) at Day 1, 8 and 15 - Part 1

End point title	Percent Change From Baseline in Phosphorylation Inhibition of Crk Like Protein (CrkL) at Day 1, 8 and 15 - Part 1[39]

End point description:

CrkL is a protein, phosphorylation of which has been shown to correlate with CML cell growth; and conversely inhibition of their phosphorylation correlates with inhibition of tumor cell growth. Phosphorylation of CrkL was monitored in whole blood cells, as well as in the CD3+ (T cell), CD19+ (B cell) and CD34+ (blast cell) compartments by using FACS flow cytometry.9999 = not estimable, standard deviation was not estimable since only 1 participant was evaluable.
Evaluable population included all enrolled participants who received at least 1 dose of study medication and had an adequate baseline efficacy assessment. 'N' signifies number of participants who were evaluable for this measure. n=number of participants
evaluable for this measure at specified time points for each arm group respectively.

End point type	Secondary

End point timeframe:

6 hours post-dose on Day 1, 0 (pre-dose), 6 hours post-dose on Day 8, 15

Notes:

[39] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 1 are presented for this endpoint.

End point values	Bosutinib 400 mg (Part 1)	Bosutinib 500 mg (Part 1)	Bosutinib 600 mg (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	3	9	
Units: percent change				
arithmetic mean (standard deviation)				
Day 1: post-dose (n=1, 1, 9)	-34.66 (± 9999)	287.52 (± 9999)	97.79 (± 283.61)	
Day 8: pre-dose (n=1, 1, 9)	562.48 (± 9999)	170.83 (± 9999)	3.88 (± 128.97)	
Day 8: post-dose (n=1, 1, 9)	528.62 (± 9999)	429.79 (± 9999)	143.57 (± 289.18)	
Day 15: pre-dose (n=1, 2, 7)	177.87 (± 9999)	-44.64 (± 8.56)	119.23 (± 170.91)	
Day 15: post-dose (n=1, 3, 7)	-49.85 (± 9999)	-21.13 (± 57.91)	138.45 (± 278.24)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Major Cytogenetic Response (MCyR) in Chronic Phase Second-line and Chronic Phase Third-line CML Population - Part 2

End point title	Percentage of Participants With Major Cytogenetic Response (MCyR) in Chronic Phase Second-line and Chronic Phase Third-line CML Population - Part 2[40]

End point description:

CyR is based on the prevalence of Ph+ cells. MCyR was categorized as either CCyR or PCyR. CCyR was achieved when there was 0% Ph+ cells from at least 20 metaphases from conventional bone marrow cytogenetics or <1% positive cells from at least 200 cells analyzed from FISH. PCyR was achieved when 1 to 35% Ph+ cells were present.
Cytogenetic evaluable population included all enrolled participants who received at least one dose of study medication and had an adequate baseline cytogenetic assessment.

End point type	Secondary

End point timeframe:

Week 12, thereafter assessed every 12 weeks up to 2 years then every 24 weeks thereafter up to Year 4 (CP3L) or Year 5 (CP2L)

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	182	80	5	36
Units: percentage of participants				
number (confidence interval 95%)	58.8 (51.3 to 66)	61.3 (49.7 to 71.9)	40 (5.3 to 85.3)	38.9 (23.1 to 56.5)

End point values	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	26		
Units: percentage of participants				
number (confidence interval 95%)	42.2 (27.7 to 57.9)	38.5 (20.2 to 59.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Retaining an Attained/Maintained Major Cytogenetic Response (MCyR) at Year 5 in Chronic Phase Second-line CML - Part 2

End point title	Kaplan-Meier Estimate of Retaining an Attained/Maintained Major Cytogenetic Response (MCyR) at Year 5 in Chronic Phase Second-line CML - Part 2[41]

End point description:

MCyR was categorized as either CCyR or PCyR. CCyR was achieved when there was 0% Ph+ cells from at least 20 metaphases from conventional bone marrow cytogenetics or <1% positive cells from at least 200 cells analyzed from FISH. PCyR was achieved when 1 to 35% Ph+ cells were present. The Kaplan-Meier probability of retaining an attained/maintained MCyR at Year 5 is reported. Median durations were not reached as of the minimum follow-up. Duration of response in weeks =(date of confirmed loss of first attained response or last valid cytogenetic assessment for those censored - date of first attained response)/7.
Subgroup of participants from evaluable population who had MCyR.

End point type	Secondary

End point timeframe:

From first MCyR to loss of MCyR or censoring, assessed every 12 weeks up to 2 years and then every 24 weeks thereafter

Notes:

[41] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	49		
Units: % probability of retaining MCyR				
number (confidence interval 95%)	67.2 (56.8 to 75.6)	79.8 (63.1 to 89.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Achieve Major Cytogenetic Response (MCyR) in Chronic Phase Second-line CML for Responders Only - Part 2

End point title	Time to Achieve Major Cytogenetic Response (MCyR) in Chronic Phase Second-line CML for Responders Only - Part 2[42]

End point description:

MCyR was categorized as either CCyR or PCyR. CCyR was achieved when there was 0% Ph+ cells from at least 20 metaphases from conventional bone marrow cytogenetics or <1% positive cells from at least 200 cells analyzed from FISH. PCyR was achieved when 1 to 35% Ph+ cells were present. Time to MCyR was the interval from the date of first dose of study medication until the first date of achieving a given response. Time to response in weeks equals (=) (event date minus (-) first dose date plus (+) 1)divided (/)7, where the event date is the non-missing date of the first attained response for responders only. Cytogenetic evaluable population included all enrolled participants who received at least one dose of study medication and had an adequate baseline cytogenetic assessment.

End point type	Secondary

End point timeframe:

Week 12, thereafter assessed every 12 weeks up to 2 years then every 24 weeks thereafter

Notes:

[42] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	49		
Units: weeks				
median (confidence interval 95%)	12.3 (12.1 to 24)	12.1 (12 to 12.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Maintaining Complete Hematologic Response (CHR) at Year 4 (CP3L and ADV) or Year 5 (CP2L) for Responders Only, Part 2 - Hematologic Evaluable Population

End point title	Kaplan-Meier Estimate of Maintaining Complete Hematologic Response (CHR) at Year 4 (CP3L and ADV) or Year 5 (CP2L) for Responders Only, Part 2 - Hematologic Evaluable Population[43]

End point description:

Hematologic response: if participants met all of the following criteria of CHR: White Blood Cells equal to or less than (≤) institutional upper limit of normal, no peripheral blood blasts or promyelocytes, myelocytes+metamyelocytes less than (<)5% in blood, absolute neutrophil count greater than or equal to (≥) 1.0×10^9 per liter (/L) , platelets ≥100×10^9/L & <450×10^9/L, <20% basophils in blood & no extramedually involvement (including hepato- or splenomegaly), ≤5% BM blasts (ADV only & applicable to CP if BM aspirate was performed). The duration of CHR was defined as the interval from the first date of response until the first date of confirmed loss of response. Duration of response in weeks =(date of confirmed loss of attained response or last valid hematologic assessment for those censored - date of first confirmed response)/7. The Kaplan-Meier estimate of maintaining CHR at the end of minimum follow-up is presented (CP2L: Year 5; CP3L & ADV: Year 4).
-9999/9999 = not estimable.

End point type	Secondary

End point timeframe:

From date of first confirmed CHR to loss of CHR or censoring, assessed at Day 1 and 7 of Week 1, Day 7 of Week 2, 3, 4, 8, 12, thereafter assessed every 12 weeks up to 2 years then every 24 weeks thereafter

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	169	76	4	26
Units: % estimate of maintaining response				
number (confidence interval 95%)	61.5 (52.9 to 69.1)	78.2 (64.4 to 87.1)	50 (5.8 to 84.5)	56.5 (30.9 to 75.8)

End point values	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)	Bosutinib 500 mg, Ph+ ALL (Part 2)	Bosutinib 500 mg, AP-CML IM R/I (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	37	19	2	17
Units: % estimate of maintaining response				
number (confidence interval 95%)	69.9 (49.7 to 83.3)	61.9 (33.6 to 81)	100 (-9999 to 100)	47.1 (20.7 to 69.7)

End point values	Bosutinib 500 mg, AP-CML Multi-TKI R/I (Part 2)	Bosutinib 500 mg, BP-CML IM R/I (Part 2)	Bosutinib 500 mg, BP-CML Multi-TKI R/I (Part 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	7	9	1	
Units: % estimate of maintaining response				
number (confidence interval 95%)	64.3 (15.1 to 90.2)	9999 (9999 to 9999)	9999 (9999 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Complete Hematologic Response (CHR) for Responders Only, Part 2 - Hematologic Evaluable Population

End point title	Duration of Complete Hematologic Response (CHR) for Responders Only, Part 2 - Hematologic Evaluable Population[44]

End point description:

Hematologic response: if participants met all of the following criteria of CHR: White Blood Cells equal to or less than (≤) institutional upper limit of normal, no peripheral blood blasts or promyelocytes, myelocytes+metamyelocytes less than (<)5% in blood, absolute neutrophil count greater than or equal to (≥) 1.0×10^9 per liter (/L) , platelets <450×10^9/L, platelets ≥100×10^9/L, <20% basophils in blood and no extramedually involvement (including hepato- or splenomegaly), ≤5% BM blasts (required for ADV only and applicable to CP if BM aspirate was performed). The duration of CHR was defined as the interval from the first date of response until the first date of confirmed loss of response. Duration of response in weeks =(date of confirmed loss of attained response or last valid hematologic assessment for those censored - date of first confirmed response)/7.
-9999/9999 = not estimable, median duration was not reached prior to minimum follow-up period.

End point type	Secondary

End point timeframe:

From date of first confirmed CHR to loss of CHR or censoring, assessed at Day 1 and 7 of Week 1, Day 7 of Week 2, 3, 4, 8, 12, thereafter assessed every 12 weeks up to 2 years then every 24 weeks thereafter

Notes:

[44] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	169	76	4	26
Units: weeks				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9.6 to 9999)	9999 (38.3 to 9999)

End point values	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)	Bosutinib 500 mg, Ph+ ALL (Part 2)	Bosutinib 500 mg, AP-CML IM R/I (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	37	19	2	17
Units: weeks				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (56 to 9999)	9999 (9999 to 9999)	138 (24 to 9999)

End point values	Bosutinib 500 mg, AP-CML Multi-TKI R/I (Part 2)	Bosutinib 500 mg, BP-CML IM R/I (Part 2)	Bosutinib 500 mg, BP-CML Multi-TKI R/I (Part 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	7	9	1	
Units: weeks				
median (confidence interval 95%)	9999 (102 to 9999)	28.6 (20.1 to 9999)	40 (-9999 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Achieve Complete Hematologic Response (CHR) for Responders Only - Part 2

End point title	Time to Achieve Complete Hematologic Response (CHR) for Responders Only - Part 2[45]

End point description:

The time to CHR was measured from the date of first dosing to the first date of response. Time to response in weeks = (event date - first dose date plus 1)/7, where the event date is the non-missing date of the first attained response for responders only.
9999 = not estimable
Hematologic evaluable population included all enrolled participants who received at least one dose of study medication and had an adequate baseline hematologic assessment responders only.

End point type	Secondary

End point timeframe:

Day 1 and 7 of Week 1, Day 7 of Week 2, 3, 4, 8, 12, thereafter assessed every 12 weeks up to 2 years then every 24 weeks thereafter

Notes:

[45] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	169	76	4	26
Units: weeks				
median (confidence interval 95%)	2 (1.1 to 2.1)	1.3 (1.1 to 2.1)	1.6 (1.1 to 2.1)	1.2 (1.1 to 3)

End point values	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)	Bosutinib 500 mg, Ph+ ALL (Part 2)	Bosutinib 500 mg, AP-CML IM R/I (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	37	19	2	17
Units: weeks				
median (confidence interval 95%)	1.3 (1.1 to 2.3)	2.4 (1.1 to 3.3)	10 (4 to 13)	12.1 (8.1 to 24)

End point values	Bosutinib 500 mg, AP-CML Multi-TKI R/I (Part 2)	Bosutinib 500 mg, BP-CML IM R/I (Part 2)	Bosutinib 500 mg, BP-CML Multi-TKI R/I (Part 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	7	9	1	
Units: weeks				
median (confidence interval 95%)	12.1 (4.3 to 72)	8 (4 to 13)	12.1 (-9999 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Incidence of Progression/Death - Part 2

End point title	Cumulative Incidence of Progression/Death - Part 2[46]

End point description:

The cumulative incidence of on-treatment progression or death adjusting for the competing risk of treatment discontinuation without the event. Disease progression was determined by the investigator as the reason for treatment discontinuation and death was due to any cause within 30 days of last dose. Duration in months = (date of PD/death or last valid cytogenetic/hematologic assessment if censored - first dose date)/30.4. 95% confidence intervals were calculated using Gray's method. One year = 12 months. 9999 = not estimable, in Part 2 participants in CP3L and ADV treatment groups were only evaluated up to Year 4.
All-treated population included all enrolled participants who received at least one dose of study medication.

End point type	Secondary

End point timeframe:

Years 1, 2, 3, 4, and 5 (CP2L only)

Notes:

[46] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	195	89	5	38
Units: percentage of participants				
number (confidence interval 95%)				
Year 1	10.8 (7.2 to 16.1)	4.5 (1.7 to 11.7)	20 (3.5 to 100)	23.7 (13.4 to 41.9)
Year 2	19 (14.2 to 25.4)	6.7 (3.1 to 14.6)	40 (13.7 to 100)	23.7 (13.4 to 41.9)
Year 3	22.1 (16.9 to 28.7)	9 (4.6 to 17.4)	40 (13.7 to 100)	23.7 (13.4 to 41.9)
Year 4	22.6 (17.4 to 29.3)	9 (4.6 to 17.4)	40 (13.7 to 100)	23.7 (13.4 to 41.9)
Year 5	23.1 (17.9 to 29.8)	10.1 (5.4 to 18.8)	9999 (9999 to 9999)	9999 (9999 to 9999)

End point values	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)	Bosutinib 500 mg, Ph+ ALL (Part 2)	Bosutinib 500 mg, AP-CML IM R/I (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	50	26	24	49
Units: percentage of participants				
number (confidence interval 95%)				
Year 1	12 (5.7 to 25.4)	23.1 (11.4 to 46.6)	58.3 (41.6 to 81.8)	28.6 (18.4 to 44.5)
Year 2	14 (7 to 27.8)	30.8 (17.3 to 54.8)	58.3 (41.6 to 81.8)	42.9 (31 to 59.2)
Year 3	16 (8.5 to 30.2)	34.6 (20.4 to 58.7)	58.3 (41.6 to 81.8)	44.9 (32.9 to 61.2)
Year 4	16 (8.5 to 30.2)	34.6 (20.4 to 58.7)	58.3 (41.6 to 81.8)	44.9 (32.9 to 61.2)
Year 5	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)

End point values	Bosutinib 500 mg, AP-CML Multi-TKI R/I (Part 2)	Bosutinib 500 mg, BP-CML IM R/I (Part 2)	Bosutinib 500 mg, BP-CML Multi-TKI R/I (Part 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	36	28	
Units: percentage of participants				
number (confidence interval 95%)				
Year 1	20 (9.8 to 40.9)	47.2 (33.4 to 66.7)	71.4 (56.5 to 90.3)	
Year 2	23.3 (12.2 to 44.6)	50 (36.1 to 69.3)	71.4 (56.5 to 90.3)	
Year 3	26.7 (14.7 to 48.3)	50 (36.1 to 69.3)	75 (60.6 to 92.9)	
Year 4	26.7 (14.7 to 48.3)	50 (36.1 to 69.3)	75 (60.6 to 92.9)	
Year 5	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Overall Survival (OS) - Part 2

End point title	Kaplan-Meier Estimate of Overall Survival (OS) - Part 2[47]

End point description:

OS was based on Kaplan-Meier method. Survival was defined as the time period from the date of first dose of bosutinib to the date of death or date of last contact for those censored. One year = 12 months. 9999 = not estimable, in Part 2 participants in CP3L and ADV treatment groups were only evaluated up to Year 4.

All-treated population included all enrolled participants who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Years 1, 2, 3, 4, and 5 (CP2L only)

Notes:

[47] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	195	89	5	38
Units: percentage of participants				
number (confidence interval 95%)				
Year 1	96.3 (92.5 to 98.2)	98.9 (92.1 to 99.8)	100 (100 to 100)	85.8 (69.2 to 93.8)
Year 2	88.2 (82.7 to 92.1)	97.7 (91 to 99.4)	80 (20.4 to 96.9)	79.7 (62 to 89.8)
Year 3	84.1 (77.8 to 88.7)	93 (83.9 to 97.1)	80 (20.4 to 96.9)	66.1 (44.5 to 80.9)
Year 4	81.5 (74.7 to 86.6)	93 (83.9 to 97.1)	80 (20.4 to 96.9)	66.1 (44.5 to 80.9)
Year 5	80.6 (73.6 to 85.9)	88.4 (76.6 to 94.5)	9999 (9999 to 9999)	9999 (9999 to 9999)

End point values	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)	Bosutinib 500 mg, Ph+ ALL (Part 2)	Bosutinib 500 mg, AP-CML IM R/I (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	50	26	24	49
Units: percentage of participants				
number (confidence interval 95%)				
Year 1	91.8 (79.7 to 96.6)	96.2 (75.7 to 99.4)	16.7 (5.2 to 33.7)	81.3 (67.2 to 89.8)
Year 2	83.3 (69.3 to 91.3)	92.3 (72.6 to 98)	8.3 (1.4 to 23.3)	72.7 (57.6 to 83.1)
Year 3	83.3 (69.3 to 91.3)	86.5 (62.9 to 95.6)	8.3 (1.4 to 23.3)	70.1 (54.7 to 81.1)
Year 4	79.3 (63.1 to 89)	86.5 (62.9 to 95.6)	8.3 (1.4 to 23.3)	65.7 (48.6 to 78.3)
Year 5	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)

End point values	Bosutinib 500 mg, AP-CML Multi-TKI R/I (Part 2)	Bosutinib 500 mg, BP-CML IM R/I (Part 2)	Bosutinib 500 mg, BP-CML Multi-TKI R/I (Part 2)	

Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	36	28	
Units: percentage of participants				
number (confidence interval 95%)				
Year 1	72.9 (53 to 85.4)	44.3 (27.4 to 59.9)	39.3 (21.7 to 56.5)	
Year 2	59 (39.2 to 74.3)	41.3 (24.9 to 57)	25 (11.1 to 41.8)	
Year 3	45.1 (25.4 to 63)	41.3 (24.9 to 57)	16.7 (5.6 to 32.9)	
Year 4	45.1 (25.4 to 63)	20.7 (2 to 53.2)	16.7 (5.6 to 32.9)	
Year 5	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Confirmed Complete Hematologic Response (CHR) - Part 2

End point title	Percentage of Participants With Confirmed Complete Hematologic Response (CHR) - Part 2[48]

End point description:

Hematologic response: if participants met all of the following criteria of CHR: White Blood Cells ≤ institutional upper limit of normal, no peripheral blood blasts or promyelocytes, myelocytes+metamyelocytes <5% in blood, absolute neutrophil count ≥ 1.0×10^9/L , platelets <450×10^9/L, platelets ≥100×10^9/L, <20% basophils in blood and no extramedually involvement (including hepato- or splenomegaly), ≤5% BM blasts (required for ADV only and applicable to CP if BM aspirate was performed).
Hematologic evaluable population included all enrolled participants who received at least one dose of study medication and had an adequate baseline hematologic assessment.

End point type	Secondary

End point timeframe:

Day 1 and 7 of Week 1, Day 7 of Week 2, 3, 4, 8, 12, thereafter assessed every 12 weeks up to 2 years then every 24 weeks thereafter

Notes:

[48] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	194	89	5	38
Units: percentage of participants				
number (confidence interval 95%)	87.1 (81.6 to 91.5)	85.4 (76.3 to 92)	80 (28.4 to 99.5)	68.4 (51.3 to 82.5)

End point values	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)	Bosutinib 500 mg, Ph+ ALL (Part 2)	Bosutinib 500 mg, AP-CML IM R/I (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	49	25	22	43
Units: percentage of participants				
number (confidence interval 95%)	75.5 (61.1 to 86.7)	76 (54.9 to 90.6)	9.1 (1.1 to 29.2)	39.5 (25 to 55.6)

End point values	Bosutinib 500 mg, AP-CML Multi-TKI R/I (Part 2)	Bosutinib 500 mg, BP-CML IM R/I (Part 2)	Bosutinib 500 mg, BP-CML Multi-TKI R/I (Part 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	29	34	26	
Units: percentage of participants				
number (confidence interval 95%)	24.1 (10.3 to 43.5)	26.5 (12.9 to 44.4)	3.8 (0.1 to 19.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Overall Hematologic Response (OHR) by Week 48 in Advanced Leukemia Hematologic Evaluable Population - Part 2

End point title	Percentage of Participants With Overall Hematologic Response (OHR) by Week 48 in Advanced Leukemia Hematologic Evaluable Population - Part 2[49]

End point description:

OHR included CHR, no evidence of leukemia (≤5% bone marrow blasts, no peripheral blood blasts or promyelocytes, <5% myelocytes + metamyelocytes in blood, white blood cells ≤ institutional upper limit of normal, 450x10^9/L > platelets > 20x10^9/L, absolute neutrophil count ≥0.5x10^9/L, <20% basophils in blood, no extramedullary involvement [including liver or spleen]), minor hematologic response (acute lymphoblastic leukemia [ALL] patients only, defined as <15% blasts in marrow & blood, <30% blasts + promyelocytes in marrow & blood, <20% basophils in peripheral blood & no extramedullary disease other than spleen & liver) or return to chronic phase (AP/BP participants, defined as <15% blasts in both peripheral blood &bone marrow, <30% blasts + promyelocytes in both peripheral blood & bone marrow, <20% basophils in both peripheral blood & bone marrow, no extramedullary Involvement other than liver or spleen). Participants had to meet at least 1 criterion.

End point type	Secondary

End point timeframe:

Day 1 and 7 of Week 1, Day 7 of Week 2, 3, 4, 8, 12, thereafter assessed every 12 weeks up to 1 year

Notes:

[49] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, Ph+ ALL (Part 2)	Bosutinib 500 mg, AP-CML IM R/I (Part 2)	Bosutinib 500 mg, AP-CML Multi-TKI R/I (Part 2)	Bosutinib 500 mg, BP-CML IM R/I (Part 2)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	43	29	34
Units: percentage of participants				
number (confidence interval 95%)	9.1 (1.1 to 29.2)	67.4 (51.5 to 80.9)	41.4 (23.5 to 61.1)	38.2 (22.2 to 56.4)

End point values	Bosutinib 500 mg, BP-CML Multi-TKI R/I (Part 2)			
Subject group type	Subject analysis set			
Number of subjects analysed	26			
Units: percentage of participants				
number (confidence interval 95%)	15.4 (4.4 to 34.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Treatment-Emergent Adverse Events (AEs) or Serious Adverse Events (SAEs)

End point title	Percentage of Participants With Treatment-Emergent Adverse Events (AEs) or Serious Adverse Events (SAEs)[50]

End point description:

An AE was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent are events between first dose of study drug and up to 30 days after last dose that were absent before treatment or that worsened relative to pretreatment state. Safety population included all participants who receive at least one dose of study medication.

End point type	Secondary

End point timeframe:

Baseline up to follow up visit (30 days after last dose of study treatment)

Notes:

[50] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	195	89	5	38
Units: percentage of participants				

number (not applicable)				
AEs	99.5	100	100	100
SAEs	41.5	38.2	20	39.5

End point values	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)	Bosutinib 500 mg, Ph+ ALL (Part 2)	Bosutinib 500 mg, AP-CML IM R/I (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	50	26	24	49
Units: percentage of participants				
number (not applicable)				
AEs	100	100	95.8	100
SAEs	38	19.2	70.8	49

End point values	Bosutinib 500 mg, AP-CML Multi-TKI R/I (Part 2)	Bosutinib 500 mg, BP-CML IM R/I (Part 2)	Bosutinib 500 mg, BP-CML Multi-TKI R/I (Part 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	36	28	
Units: percentage of participants				
number (not applicable)				
AEs	100	97.2	100	
SAEs	63.3	55.6	60.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Potentially Clinically Important (PCI) Adverse Events (AEs)

End point title	Duration of Potentially Clinically Important (PCI) Adverse Events (AEs)[51]

End point description:

An AE was any untoward medical occurrence attributed to study drug in a participant who received study drug. The event did not necessarily have a causal relationship with the treatment. PCI AEs included anemia, alanine aminotranferase (ALT), aspartate aminotransferase (AST), cardiac, diarrhea, edema, effusion, gastrointestinal, hemorrhage, hypersensitivity, hypertension, infection, liver, myelosuppression, nausea, neutropenia, rash, renal, thrombocytopenia, vomiting, and vascular events. Duration of AE was calculated as (stop date minus start date) plus 1 for non-missing and non-partial dates.
9999 = no events therefore duration not available.
Safety population included all participants who receive at least one dose of study medication.

End point type	Secondary

End point timeframe:

Baseline up to follow-up visit (30 days after last dose of study treatment)

Notes:

[51] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	195	89	5	38
Units: days				
median (full range (min-max))				
Anaemia	14 (1 to 1373)	36 (2 to 688)	38 (38 to 38)	19 (1 to 284)
ALT	29 (1 to 775)	15 (1 to 344)	9999 (9999 to 9999)	21.5 (7 to 236)
AST	29 (1 to 803)	13.5 (1 to 330)	9999 (9999 to 9999)	18 (14 to 22)
Diarrhoea	1 (1 to 2174)	2 (1 to 1121)	2 (1 to 59)	2 (1 to 189)
Effusion	18.5 (1 to 1428)	29 (5 to 657)	79.5 (14 to 421)	20 (7 to 842)
Infection	10 (1 to 1026)	9.5 (1 to 546)	11.5 (1 to 46)	8 (1 to 85)
Nausea	2 (1 to 972)	4 (1 to 446)	4 (1 to 7)	2 (1 to 168)
Neutropenia	23 (1 to 506)	15 (1 to 337)	23 (13 to 70)	14.5 (4 to 81)
Oedema	29 (1 to 1416)	81.5 (1 to 1807)	4 (1 to 52)	1 (1 to 455)
Rash	15 (1 to 1622)	13 (1 to 965)	17 (7 to 52)	12 (1 to 348)
Renal events	27 (1 to 831)	190 (7 to 903)	1167 (1167 to 1167)	162 (21 to 299)
Thrombocytopenia	22 (1 to 1762)	15 (1 to 1541)	38.5 (14 to 120)	15 (1 to 336)
Vomiting	1 (1 to 165)	1 (1 to 36)	9999 (9999 to 9999)	1 (1 to 141)
Cardiac events	11 (1 to 1428)	6 (1 to 657)	9999 (9999 to 9999)	7.5 (1 to 842)
Vascular events	3.5 (1 to 277)	6 (1 to 59)	9999 (9999 to 9999)	10.5 (3 to 18)
Hypertension	16 (1 to 1343)	1 (1 to 1659)	9999 (9999 to 9999)	7 (7 to 7)
Gastrointestinal events	1 (1 to 2174)	2 (1 to 1121)	2 (1 to 59)	2 (1 to 189)
Haemorrhage	10 (1 to 862)	16 (1 to 131)	23 (23 to 23)	4 (1 to 11)
Hypersensitivity	9 (6 to 38)	8 (7 to 9)	9999 (9999 to 9999)	7 (1 to 28)
Liver	29 (1 to 803)	16 (1 to 344)	8 (8 to 8)	25.5 (7 to 236)
Myelosuppression	22 (1 to 1762)	18 (1 to 1541)	28 (13 to 120)	15 (1 to 336)

End point values	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)	AP-CML Total (Part 2)	BP-CML Total (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	26	79	64
Units: days				

median (full range (min-max))				
Anaemia	13 (6 to 271)	61 (6 to 335)	12.5 (1 to 502)	4 (1 to 52)
ALT	8 (5 to 87)	21 (4 to 42)	21.5 (7 to 252)	7.5 (1 to 41)
AST	8.5 (8 to 22)	15 (8 to 21)	14 (1 to 188)	2 (2 to 2)
Diarrhoea	2 (1 to 413)	1 (1 to 289)	2 (1 to 910)	2 (1 to 211)
Effusion	28 (1 to 907)	20 (5 to 258)	21 (4 to 1536)	58 (11 to 101)
Infection	9 (2 to 366)	8 (1 to 183)	9 (1 to 281)	9.5 (1 to 78)
Nausea	14 (1 to 713)	2 (1 to 42)	6 (1 to 247)	6.5 (1 to 274)
Neutropenia	21 (3 to 504)	26 (7 to 92)	8 (1 to 252)	5 (1 to 52)
Oedema	12.5 (2 to 774)	28 (3 to 316)	88.5 (2 to 670)	11 (1 to 214)
Rash	19 (1 to 1612)	12.5 (1 to 150)	13 (1 to 428)	7.5 (1 to 218)
Renal events	11 (1 to 203)	56.5 (29 to 84)	26 (3 to 1403)	9 (1 to 27)
Thrombocytopenia	15 (2 to 420)	21.5 (6 to 350)	11.5 (1 to 889)	5 (1 to 176)
Vomiting	2 (1 to 59)	7 (1 to 39)	1 (1 to 128)	1 (1 to 41)
Cardiac events	22 (1 to 907)	1 (1 to 1)	14 (1 to 1536)	3 (1 to 19)
Vascular events	1.5 (1 to 266)	10 (10 to 10)	2 (1 to 22)	1 (1 to 14)
Hypertension	1 (1 to 418)	9999 (9999 to 9999)	5 (1 to 204)	9999 (9999 to 9999)
Gastrointestinal events	2 (1 to 713)	2 (1 to 289)	2 (1 to 910)	3 (1 to 274)
Haemorrhage	27.5 (1 to 190)	7.5 (1 to 58)	6 (1 to 147)	4 (1 to 28)
Hypersensitivity	6 (1 to 15)	5 (1 to 9)	1 (1 to 1)	9999 (9999 to 9999)
Liver	9 (5 to 136)	21 (3 to 82)	16 (1 to 252)	8 (1 to 441)
Myelosuppression	15 (2 to 504)	27 (6 to 769)	11.5 (1 to 889)	5 (1 to 376)

End point values	Bosutinib 500 mg, Ph+ ALL (Part 2)			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: days				
median (full range (min-max))				
Anaemia	7 (1 to 20)			
ALT	3 (1 to 5)			
AST	5 (5 to 5)			
Diarrhoea	3 (1 to 500)			
Effusion	5 (4 to 25)			
Infection	9 (1 to 39)			
Nausea	9 (1 to 31)			
Neutropenia	6.5 (5 to 8)			
Oedema	5 (1 to 8)			
Rash	12 (1 to 33)			
Renal events	12 (12 to 12)			
Thrombocytopenia	9 (3 to 43)			
Vomiting	1.5 (1 to 9)			
Cardiac events	1.5 (1 to 2)			
Vascular events	1 (1 to 19)			
Hypertension	2 (2 to 2)			
Gastrointestinal events	4 (1 to 500)			
Haemorrhage	3.5 (1 to 21)			

Hypersensitivity	9999 (9999 to 9999)			
Liver	5 (1 to 9)			
Myelosuppression	7 (1 to 43)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Change From Baseline in Laboratory Tests Results

End point title	Number of Participants With Change From Baseline in Laboratory Tests Results[52]

End point description:

Laboratory assessments included urinalysis, complete blood count (CBC), prothrombin time/partial prothromboplastin time (PT/PPT), international normalized ratio (INR), blood chemistry and serum pregnancy test (β-HCG). Parameters of special interest included liver function tests and those related to myelosuppression. Potentially clinically important (PCI) laboratory values were defined as National Cancer Institute Common Terminology Criteria for Adverse Events Version 3.0 (NCI CTCAE v3.0) grade 3 or higher. Maximum CTCAE grade, and only participants who shifted to Grade 3/4 on-treatment, are reported.
Safety population included all participants who receive at least one dose of study medication.

End point type	Secondary

End point timeframe:

Week 1, 2, 3, 4, 8, 12, thereafter assessed every 12 weeks up to 2 years then every 24 weeks thereafter

Notes:

[52] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	195	89	5	38
Units: Percentage of Participants				
number (not applicable)				
Hemoglobin: shift from Normal to Grade 3	0.5	1.1	0	0
Hemoglobin: shift from Normal to Grade 4	1	0	0	0
Hemoglobin: shift from Grade 1 to Grade 3	3.6	10.1	0	2.6
Hemoglobin: shift from Grade 1 to Grade 4	1.5	0	0	0
Hemoglobin: shift from Grade 2 to Grade 3	3.1	6.7	0	7.9
Hemoglobin: shift from Grade 2 to Grade 4	2.1	1.1	0	0
Hemoglobin: shift from Grade 3 to Grade 4	0.5	0	0	0
Absolute neutrophils (ANC): Normal to Grade 3	7.2	9	0	5.3

ANC: shift from Normal to Grade 4	2.1	3.4	20	7.9
ANC: shift from Grade 1 to Grade 3	0	2.2	0	0
ANC: shift from Grade 1 to Grade 4	0.5	0	0	2.6
ANC: shift from Grade 2 to Grade 3	1	3.4	0	2.6
ANC: shift from Grade 2 to Grade 4	0	0	0	0
ANC: shift from Grade 3 to Grade 4	0	1.1	0	0
Platelet count: shift from Normal to Grade 3	13.3	13.5	0	15.8
Platelet count: shift from Normal to Grade 4	3.6	7.9	0	0
Platelet count: shift from Grade 1 to Grade 3	3.6	5.6	0	2.6
Platelet count: shift from Grade 1 to Grade 4	1.5	1.1	0	2.6
Platelet count: shift from Grade 2 to Grade 3	0.5	2.2	20	0
Platelet count: shift from Grade 2 to Grade 4	0.5	0	0	0
Platelet count: shift from Grade 3 to Grade 4	1	0	0	0
ALT: shift from Normal to Grade 3	8.7	12.4	0	0
ALT: shift from Grade 1 to Grade 3	1	0	0	0
AST: shift from Normal to Grade 3	4.1	7.9	0	0
AST: shift from Normal to Grade 4	0	0	0	0
AST: shift from Grade 1 to Grade 3	0	0	0	0
ALP: shift from Normal to Grade 3	0	0	0	0
ALP: shift from Grade 1 to Grade 3	0	0	0	0
Total bilirubin: shift from Normal to Grade 3	0	0	0	0
ALT: shift from Normal to Grade 4	0	2.2	0	0
Total bilirubin: shift from Grade 2 to Grade 3	0	0	0	0

End point values	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)	AP-CML Total (Part 2)	BP-CML Total (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	26	79	64
Units: Percentage of Participants				
number (not applicable)				
Hemoglobin: shift from Normal to Grade 3	0	3.8	5.1	1.6
Hemoglobin: shift from Normal to Grade 4	0	0	0	0
Hemoglobin: shift from Grade 1 to Grade 3	0	0	7.6	6.3
Hemoglobin: shift from Grade 1 to Grade 4	4	0	1.3	3.1
Hemoglobin: shift from Grade 2 to Grade 3	0	0	10.1	15.6
Hemoglobin: shift from Grade 2 to Grade 4	4	0	2.5	4.7
Hemoglobin: shift from Grade 3 to Grade 4	0	0	5.1	4.7

Absolute neutrophils (ANC): Normal to Grade 3	4	11.5	10.1	3.1
ANC: shift from Normal to Grade 4	4	3.8	2.5	3.1
ANC: shift from Grade 1 to Grade 3	0	0	2.5	7.8
ANC: shift from Grade 1 to Grade 4	2	0	1.3	20.3
ANC: shift from Grade 2 to Grade 3	2	0	3.8	0
ANC: shift from Grade 2 to Grade 4	0	0	1.3	3.1
ANC: shift from Grade 3 to Grade 4	2	0	0	4.7
Platelet count: shift from Normal to Grade 3	12	7.7	11.4	4.7
Platelet count: shift from Normal to Grade 4	8	15.4	7.6	1.6
Platelet count: shift from Grade 1 to Grade 3	2	3.8	5.1	3.1
Platelet count: shift from Grade 1 to Grade 4	4	0	6.3	6.3
Platelet count: shift from Grade 2 to Grade 3	2	0	3.8	4.7
Platelet count: shift from Grade 2 to Grade 4	0	0	1.3	4.7
Platelet count: shift from Grade 3 to Grade 4	2	0	5.1	10.9
ALT: shift from Normal to Grade 3	10	15.4	5.1	1.6
ALT: shift from Grade 1 to Grade 3	0	0	3.8	0
AST: shift from Normal to Grade 3	0	7.7	2.5	1.6
AST: shift from Normal to Grade 4	0	3.8	0	0
AST: shift from Grade 1 to Grade 3	2	0	2.5	0
ALP: shift from Normal to Grade 3	0	0	1.3	0
ALP: shift from Grade 1 to Grade 3	0	0	0	1.6
Total bilirubin: shift from Normal to Grade 3	2	0	0	6.3
ALT: shift from Normal to Grade 4	0	3.8	0	0
Total bilirubin: shift from Grade 2 to Grade 3	2	0	0	0

End point values	Bosutinib 500 mg, Ph+ ALL (Part 2)			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Percentage of Participants				
number (not applicable)				
Hemoglobin: shift from Normal to Grade 3	0			
Hemoglobin: shift from Normal to Grade 4	0			
Hemoglobin: shift from Grade 1 to Grade 3	8.3			
Hemoglobin: shift from Grade 1 to Grade 4	0			
Hemoglobin: shift from Grade 2 to Grade 3	16.7			
Hemoglobin: shift from Grade 2 to Grade 4	4.2			

Hemoglobin: shift from Grade 3 to Grade 4	0			
Absolute neutrophils (ANC): Normal to Grade 3	0			
ANC: shift from Normal to Grade 4	0			
ANC: shift from Grade 1 to Grade 3	12.5			
ANC: shift from Grade 1 to Grade 4	4.2			
ANC: shift from Grade 2 to Grade 3	0			
ANC: shift from Grade 2 to Grade 4	8.3			
ANC: shift from Grade 3 to Grade 4	8.3			
Platelet count: shift from Normal to Grade 3	4.2			
Platelet count: shift from Normal to Grade 4	0			
Platelet count: shift from Grade 1 to Grade 3	4.2			
Platelet count: shift from Grade 1 to Grade 4	0			
Platelet count: shift from Grade 2 to Grade 3	0			
Platelet count: shift from Grade 2 to Grade 4	0			
Platelet count: shift from Grade 3 to Grade 4	29.2			
ALT: shift from Normal to Grade 3	0			
ALT: shift from Grade 1 to Grade 3	0			
AST: shift from Normal to Grade 3	0			
AST: shift from Normal to Grade 4	0			
AST: shift from Grade 1 to Grade 3	0			
ALP: shift from Normal to Grade 3	0			
ALP: shift from Grade 1 to Grade 3	0			
Total bilirubin: shift from Normal to Grade 3	4.2			
ALT: shift from Normal to Grade 4	0			
Total bilirubin: shift from Grade 2 to Grade 3	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With On-treatment PCI Change From Baseline in Electrocardiogram (ECG) Findings

End point title	Number of Participants With On-treatment PCI Change From Baseline in Electrocardiogram (ECG) Findings[53]

End point description:

Criteria for PCI changes in ECG (12-lead) were defined as: no sinus rhythm; PR interval >=220 msec and increase of >=20 msec; QRS interval >=120 msec; QT interval corrected using the Fridericia formula (QTcF) and QT interval corrected using the Bazett formula (QTcB) >500 msec or increase of >60 msec; heart rate <=45 beats per minute (bpm) or >=120 bpm or decrease/increase of >=15 bpm. Safety population included all participants who receive at least one dose of study medication. 'N' (Number of Participants Analyzed) signifies number of participants who were evaluable for this measure.

End point type	Secondary

End point timeframe:

Baseline, 0 (pre-dose), 2, 4, 6 hours on Day 1, 0 (pre-dose), 2, 4, 6, 20-23 hours on Day 21, and end of

treatment visit

Notes:

[53] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	195	89	5	37
Units: Percentage of participants				
number (not applicable)	32.3	23.6	20	24.3

End point values	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)	AP-CML Total (Part 2)	BP-CML Total (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	26	78	62
Units: Percentage of participants				
number (not applicable)	22	23.1	39.7	59.7

End point values	Bosutinib 500 mg, Ph+ ALL (Part 2)			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: Percentage of participants				
number (not applicable)	34.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Change From Baseline in Findings of Chest x-ray

End point title	Number of Participants With Change From Baseline in Findings of Chest x-ray[54]

End point description:

End point type	Secondary

End point timeframe:

Baseline, Week 8, and end of treatment

Notes:

[54] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[55]	0[56]	0[57]	0[58]
Units: participants				

Notes:

[55] - Data not statistically summarized, but collected and reported in individual listings as planned.

[56] - Data not statistically summarized, but collected and reported in individual listings as planned.

[57] - Data not statistically summarized, but collected and reported in individual listings as planned.

[58] - Data not statistically summarized, but collected and reported in individual listings as planned.

End point values	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)	AP-CML Total (Part 2)	BP-CML Total (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[59]	0[60]	0[61]	0[62]
Units: participants				

Notes:

[59] - Data not statistically summarized, but collected and reported in individual listings as planned.

[60] - Data not statistically summarized, but collected and reported in individual listings as planned.

[61] - Data not statistically summarized, but collected and reported in individual listings as planned.

[62] - Data not statistically summarized, but collected and reported in individual listings as planned.

End point values	Bosutinib 500 mg, Ph+ ALL (Part 2)			
Subject group type	Reporting group			
Number of subjects analysed	0[63]			
Units: participants				

Notes:

[63] - Data not statistically summarized, but collected and reported in individual listings as planned.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Received Concomitant Medications for Management of Adverse Events (AEs)

End point title	Number of Participants Who Received Concomitant Medications for Management of Adverse Events (AEs)[64]

End point description:

Number of participants taking any non-study medications which were administered from Study Day 1 to 30 days after last dose of study treatment as a management of an AE are reported.
Safety population included all participants who receive at least one dose of study medication.

End point type	Secondary

End point timeframe:

Baseline up to end of treatment

Notes:

[64] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	195	89	5	38
Units: participants				
ALT	7	3	0	0
AST	5	3	0	2
Anemia	6	8	2	2
Cardiac events	13	4	0	2
Gastrointestinal toxicity - Diarrhoea	120	46	2	22
Effusion	11	5	1	3
Haemorrhage	12	3	0	1
Hypertension	15	4	0	2
Hypersensitivity reactions	5	2	0	4
Infection	92	39	4	11
Hepatic events	10	5	0	0
Gastrointestinal toxicity - Nausea	33	25	1	11
Neutropenia	2	5	1	5
Rash	44	37	2	8
Oedema	13	9	1	3
Renal	2	2	0	0
Thrombocytopenia	4	2	3	10
Vascular events	6	3	0	0
Gastrointestinal toxicity - Vomiting	25	9	0	5

End point values	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)	AP-CML Total (Part 2)	BP-CML Total (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	26	79	64
Units: participants				
ALT	0	1	1	0
AST	3	4	2	0
Anemia	2	1	6	1
Cardiac events	6	0	7	2
Gastrointestinal toxicity - Diarrhoea	26	14	44	22
Effusion	9	1	9	2
Haemorrhage	0	1	4	6
Hypertension	4	1	7	2
Hypersensitivity reactions	2	2	1	1

Infection	18	10	37	30
Hepatic events	0	2	3	3
Gastrointestinal toxicity - Nausea	10	8	19	23
Neutropenia	1	1	6	5
Rash	16	3	20	9
Oedema	3	0	7	7
Renal	1	0	4	3
Thrombocytopenia	19	13	3	3
Vascular events	3	0	2	1
Gastrointestinal toxicity - Vomiting	7	4	17	14

End point values	Bosutinib 500 mg, Ph+ ALL (Part 2)			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: participants				
ALT	0			
AST	0			
Anemia	1			
Cardiac events	1			
Gastrointestinal toxicity - Diarrhoea	10			
Effusion	0			
Haemorrhage	3			
Hypertension	2			
Hypersensitivity reactions	0			
Infection	7			
Hepatic events	0			
Gastrointestinal toxicity - Nausea	7			
Neutropenia	2			
Rash	2			
Oedema	3			
Renal	0			
Thrombocytopenia	0			
Vascular events	0			
Gastrointestinal toxicity - Vomiting	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Change From Baseline in Eastern Cooperative Oncology Group Performance Status (ECOG-PS)

End point title	Number of Participants With Change From Baseline in Eastern Cooperative Oncology Group Performance Status (ECOG-PS)[65]

End point description:

ECOG-PS measured on-therapy (time between first dose and last dose date with a 30-day lag) assessed participant's performance status on 5 point scale: 0=Fully active/able to carry on all pre-disease

activities without restriction;1=restricted in physically strenuous activity, ambulatory/able to carry out light or sedentary work;2=ambulatory (>50% of waking hrs), capable of all self care, unable to carry out any work activities;3=capable of only limited self care, confined to bed/chair >50% of waking hrs;4=completely disabled, cannot carry on any self care, totally confined to bed/chair;5=dead.
Safety population included all participants who receive at least one dose of study medication.

End point type	Secondary

End point timeframe:

Baseline, Week 1, 2, 8, 12, thereafter assessed every 12 weeks up to 2 years then every 24 weeks thereafter

Notes:

[65] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	195	89	5	38
Units: participants				
Baseline: Grade 0, End of Treatment: Grade 0	92	36	2	21
Baseline: Grade 0, End of Treatment: Grade 1	50	25	0	5
Baseline: Grade 0, End of Treatment: Grade 2	3	3	0	0
Baseline: Grade 0, End of Treatment: Grade 3	4	2	0	1
Baseline: Grade 0, End of Treatment: Grade 4	2	0	0	0
Baseline: Grade 1, End of Treatment: Grade 0	0	0	0	2
Baseline: Grade 1, End of Treatment: Grade 1	32	13	2	7
Baseline: Grade 1, End of Treatment: Grade 2	10	6	1	1
Baseline: Grade 1, End of Treatment: Grade 3	0	2	0	0
Baseline: Grade 1, End of Treatment: Grade 4	2	0	0	0
Baseline: Grade 2, End of Treatment: Grade 0	0	0	0	0
Baseline: Grade 2, End of Treatment: Grade 1	0	0	0	0
Baseline: Grade 2, End of Treatment: Grade 2	0	1	0	0
Baseline: Grade 2, End of Treatment: Grade 3	0	0	0	0
Baseline: Grade 2, End of Treatment: Grade 4	0	0	0	0
Baseline: Missing	0	1	0	0
Baseline: Grade 0, End of Treatment: Missing	0	0	0	1
Baseline: Grade 1, End of Treatment: Missing	0	0	0	0

End point values	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)	Bosutinib 500 mg, Ph+ ALL (Part 2)	Bosutinib 500 mg, AP-CML IM R/I (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	50	26	24	49
Units: participants				
Baseline: Grade 0, End of Treatment: Grade 0	20	19	2	17
Baseline: Grade 0, End of Treatment: Grade 1	8	5	4	11
Baseline: Grade 0, End of Treatment: Grade 2	1	0	2	0
Baseline: Grade 0, End of Treatment: Grade 3	1	0	0	1
Baseline: Grade 0, End of Treatment: Grade 4	0	0	0	0
Baseline: Grade 1, End of Treatment: Grade 0	0	0	1	0
Baseline: Grade 1, End of Treatment: Grade 1	13	2	3	14
Baseline: Grade 1, End of Treatment: Grade 2	5	0	3	2
Baseline: Grade 1, End of Treatment: Grade 3	0	0	0	2
Baseline: Grade 1, End of Treatment: Grade 4	0	0	0	0
Baseline: Grade 2, End of Treatment: Grade 0	0	0	0	0
Baseline: Grade 2, End of Treatment: Grade 1	0	0	0	1
Baseline: Grade 2, End of Treatment: Grade 2	0	0	4	0
Baseline: Grade 2, End of Treatment: Grade 3	0	0	0	0
Baseline: Grade 2, End of Treatment: Grade 4	0	0	1	0
Baseline: Missing	1	0	0	0
Baseline: Grade 0, End of Treatment: Missing	1	0	1	0
Baseline: Grade 1, End of Treatment: Missing	0	0	3	0

End point values	Bosutinib 500 mg, AP-CML Multi-TKI R/I (Part 2)	Bosutinib 500 mg, BP-CML IM R/I (Part 2)	Bosutinib 500 mg, BP-CML Multi-TKI R/I (Part 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	36	28	
Units: participants				
Baseline: Grade 0, End of Treatment: Grade 0	9	9	2	

Baseline: Grade 0, End of Treatment: Grade 1	5	47	2	
Baseline: Grade 0, End of Treatment: Grade 2	1	0	1	
Baseline: Grade 0, End of Treatment: Grade 3	0	0	0	
Baseline: Grade 0, End of Treatment: Grade 4	0	0	0	
Baseline: Grade 1, End of Treatment: Grade 0	1	3	1	
Baseline: Grade 1, End of Treatment: Grade 1	7	7	5	
Baseline: Grade 1, End of Treatment: Grade 2	5	0	6	
Baseline: Grade 1, End of Treatment: Grade 3	0	0	3	
Baseline: Grade 1, End of Treatment: Grade 4	1	1	0	
Baseline: Grade 2, End of Treatment: Grade 0	0	1	0	
Baseline: Grade 2, End of Treatment: Grade 1	0	0	1	
Baseline: Grade 2, End of Treatment: Grade 2	0	6	1	
Baseline: Grade 2, End of Treatment: Grade 3	1	2	1	
Baseline: Grade 2, End of Treatment: Grade 4	0	0	1	
Baseline: Missing	0	0	0	
Baseline: Grade 0, End of Treatment: Missing	0	0	1	
Baseline: Grade 1, End of Treatment: Missing	0	0	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Change From Baseline in Physical Examinations and Vital Signs

End point title	Number of Participants With Change From Baseline in Physical Examinations and Vital Signs[66]

End point description:

Number of participants with PCI physical examinations and vital signs is reported during therapy and at post therapy. Criteria for PCI change in vital signs: heart rate value of <40 beats per min and value >150 beats per min, systolic blood pressure (SBP) of <80 or >210 millimeter of mercury (mmHg), diastolic blood pressure (DBP) of <40 or >130 mmHg, temperature <32 or >40 degree centigrade, respiratory rate of <10 or >50 breaths/min and criteria for PCI change in physical examination: >=10% increase or decrease of body weight in kilogram (kg). Where no participants in a cohort fulfilled the criteria, the n is not reported (NR).
Safety population included all participants who receive at least one dose of study medication. 'N' (number of participants analyzed) signifies number of participants who were evaluable for this measure.

End point type	Secondary

End point timeframe:

Baseline up to end of treatment

Notes:

[66] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	188	81	5	35
Units: participants				
SBP >210 mmHg (n=188,81,5,35,45,25,NR,NR,NR)	2	0	0	0
Weight Increase ≥10% (n187,80,5,33,46,25,73,53,16)	30	5	1	4
Weight decrease ≥10% (n187,80,5,33,46,25,73,53,16)	41	13	0	2
SBP <80 mmHg (n=188,81,5,35,45,25,NR,NR,NR)	0	0	0	0
Temperature <32C (n=NR,NR,NR,5,34,45,25,NR,NR,NR)	0	0	0	0
Pulse <40bpm (n=180,72,NR,NR,NR,NR,NR,NR,NR)	0	1	0	0
Resp >50 breaths/min (NR,NR,5,31,42,20,NR,NR,NR)	0	0	0	0
Resp <10 breaths/min (NR,NR,5,31,42,20,NR,NR,NR)	0	0	0	0

End point values	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)	AP-CML Total (Part 2)	BP-CML Total (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	25	75	56
Units: participants				
SBP >210 mmHg (n=188,81,5,35,45,25,NR,NR,NR)	0	0	0	0
Weight Increase ≥10% (n187,80,5,33,46,25,73,53,16)	3	4	8	4
Weight decrease ≥10% (n187,80,5,33,46,25,73,53,16)	7	0	17	5
SBP <80 mmHg (n=188,81,5,35,45,25,NR,NR,NR)	0	1	0	0
Temperature <32C (n=NR,NR,NR,5,34,45,25,NR,NR,NR)	0	1	0	0
Pulse <40bpm (n=180,72,NR,NR,NR,NR,NR,NR,NR)	0	0	0	0
Resp >50 breaths/min (NR,NR,5,31,42,20,NR,NR,NR)	1	1	0	0
Resp <10 breaths/min (NR,NR,5,31,42,20,NR,NR,NR)	0	1	0	0

End point values	Bosutinib 500 mg, Ph+ ALL (Part 2)			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: participants				
SBP >210 mmHg (n=188,81,5,35,45,25,NR,NR,NR)	0			
Weight Increase ≥10% (n187,80,5,33,46,25,73,53,16)	1			
Weight decrease ≥10% (n187,80,5,33,46,25,73,53,16)	0			
SBP <80 mmHg (n=188,81,5,35,45,25,NR,NR,NR)	0			
Temperature <32C (n=NR,NR,NR,5,34,45,25,NR,NR,NR)	0			
Pulse <40bpm (n=180,72,NR,NR,NR,NR,NR,NR,NR,NR)	0			
Resp >50 breaths/min (NR,NR,5,31,42,20,NR,NR,NR)	0			
Resp <10 breaths/min (NR,NR,5,31,42,20,NR,NR,NR)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Change From Baseline in Physical Examinations and Vital Signs and Number of Participants with PCI Values

End point title	Number of Participants With Change From Baseline in Physical Examinations and Vital Signs and Number of Participants with PCI Values[67]

End point description:

Number of participants with PCI physical examinations and vital signs is reported during therapy and at post therapy. Criteria for PCI change in vital signs: heart rate value of <40 beats per min and value >150 beats per min, SBP of <80 or >210 mmHg, DBP of <40 or >130 mmHg, temperature <32 or >40 degree centigrade, respiratory rate of <10 or >50 breaths/min and criteria for PCI change in physical examination: >=10% increase or decrease of body weight in kilogram (kg). Where no participants in a cohort fulfilled the criteria, the n is not reported (NR).
Safety population included all participants who receive at least one dose of study medication. 'N' (number of participants analyzed) signifies number of participants who were evaluable for this measure.

End point type	Secondary

End point timeframe:

Post-therapy

Notes:

[67] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	16	1	2
Units: participants				
Pulse <40 bpm (n=24,13,NR,NR,NR,NR,NR,NR,NA)	1	0	0	0
SBP >210 mmHg (n=NR,NR,NR,NR,NR,NR,8,3,NA)	0	0	0	0
Weight increase 10% (n=24,15,1,2,11,4,6,3,NA)	1	0	0	0
Weight decrease 10% (n=24,15,1,2,11,4,6,3,NA)	3	1	0	0

End point values	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)	AP-CML Total (Part 2)	BP-CML Total (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	4	8	3
Units: participants				
Pulse <40 bpm (n=24,13,NR,NR,NR,NR,NR,NR,NA)	0	0	0	0
SBP >210 mmHg (n=NR,NR,NR,NR,NR,NR,8,3,NA)	0	0	1	0
Weight increase 10% (n=24,15,1,2,11,4,6,3,NA)	0	0	0	1
Weight decrease 10% (n=24,15,1,2,11,4,6,3,NA)	1	0	1	0

End point values	Bosutinib 500 mg, Ph+ ALL (Part 2)			
Subject group type	Reporting group			
Number of subjects analysed	0[68]			
Units: participants				
Pulse <40 bpm (n=24,13,NR,NR,NR,NR,NR,NR,NA)				
SBP >210 mmHg (n=NR,NR,NR,NR,NR,NR,8,3,NA)				
Weight increase 10% (n=24,15,1,2,11,4,6,3,NA)				
Weight decrease 10% (n=24,15,1,2,11,4,6,3,NA)				

Notes:

[68] - No Ph+ ALL participants were analyzed post-therapy.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) - Part 2

End point title	Overall Survival (OS) - Part 2[69]

End point description:

OS was based on Kaplan-Meier method. Survival was defined as the time period from the date of first dose of bosutinib to the date of death or date of last contact for those censored. One year = 12 months. 9999 = not estimable, value not reached prior to minimum follow-up.
All-treated population included all enrolled participants who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Years 1, 2, 3, 4, and 5 (CP2L only)

Notes:

[69] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	195	89	5	38
Units: Months				
number (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (21 to 9999)	9999 (34.4 to 9999)

End point values	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)	Bosutinib 500 mg, Ph+ ALL (Part 2)	Bosutinib 500 mg, AP-CML IM R/I (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	50	26	24	49
Units: Months				
number (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)	3.6 (1.3 to 7.6)	9999 (9999 to 9999)

End point values	Bosutinib 500 mg, AP-CML Multi-TKI R/I (Part 2)	Bosutinib 500 mg, BP-CML IM R/I (Part 2)	Bosutinib 500 mg, BP-CML Multi-TKI R/I (Part 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	36	28	
Units: Months				
number (confidence interval 95%)	33.4 (14.6 to 9999)	11.2 (9.4 to 9999)	8.9 (4.1 to 17.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) - Part 2

End point title	Progression Free Survival (PFS) - Part 2[70]

End point description:

PFS was based on Kaplan-Meier method. Disease progression was determined by the investigator as the reason for treatment discontinuation and death was due to any cause within 30 days of last dose. Duration in months = (date of PD/death or last valid cytogenetic/hematologic assessment if censored first dose date)/30.4. One year = 12 months. 9999 = not estimable, value not reached prior to minimum follow-up.
All-treated population included all enrolled participants who received at least one dose of study medication.

End point type	Secondary

End point timeframe:

Years 1, 2, 3, 4, and 5 (CP2L only)

Notes:

[70] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for Part 2 are presented for this endpoint.

End point values	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	195	89	5	38
Units: Months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (0.9 to 9999)	9999 (11.1 to 9999)

End point values	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)	Bosutinib 500 mg, Ph+ ALL (Part 2)	Bosutinib 500 mg, AP-CML IM R/I (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	50	26	24	49
Units: Months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (14.1 to 9999)	1.5 (0.7 to 3.8)	20.4 (11.8 to 9999)

End point values	Bosutinib 500 mg, AP-CML Multi-TKI R/I (Part 2)	Bosutinib 500 mg, BP-CML IM R/I (Part 2)	Bosutinib 500 mg, BP-CML Multi-TKI R/I (Part 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	36	28	
Units: Months				
median (confidence interval 95%)	35.4 (14.6 to 9999)	7.9 (4 to 10.1)	1.8 (0.9 to 5.5)	

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) and serious AEs were assessed from informed consent through and including 30 days after last administration of study treatment or at the End of Treatment Visit, whichever comes last.

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as nonserious in another subject, or one subject may have experienced both a serious and nonserious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)

Reporting group description:

Bosutinib 500 mg was administered orally once-daily in participants with chronic phase second-line (CP2L) imatinib (IM) intolerant (I) chronic myelogenous leukemia (CML); who had no prior proto-oncogene tyrosine-protein kinase Src, Abl, or Src-Abl inhibitor exposure other than IM.

Reporting group title	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)

Reporting group description:

Bosutinib 500 mg was administered orally once-daily in participants with chronic phase second-line (CP2L) imatinib (IM) resistant/refractory (R) chronic myelogenous leukemia (CML); who had no prior proto-oncogene tyrosine-protein kinase sarcoma (Src), Abelson kinase (Abl), or Src-Abl inhibitor exposure other than IM.

Reporting group title	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)

Reporting group description:

Bosutinib 500 mg was administered orally once-daily in participants with chronic phase third-line (CP3L) imatinib (IM) resistant/intolerant (R/I) and dasatinib (D) resistant (R) chronic myelogenous leukemia (CML).

Reporting group title	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)

Reporting group description:

Bosutinib 500 mg was administered orally once-daily in participants with chronic phase third-line (CP3L) imatinib (IM) resistant/intolerant (R/I), dasatinib (D) and nilotinib (NI) resistant/intolerant (R/I) or imatinib (IM) resistant/intolerant (R/I) and nilotinib (NI) intolerant (I) chronic myelogenous leukemia (CML).

Reporting group title	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)

Reporting group description:

Bosutinib 500 mg was administered orally once-daily in participants with chronic phase third-line (CP3L) imatinib (IM) resistant/intolerant (R/I) and dasatinib (D) intolerant (I) chronic myelogenous leukemia (CML).

Reporting group title	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)

Reporting group description:

Bosutinib 500 mg was administered orally once-daily in participants with chronic phase third-line (CP3L) imatinib (IM) resistant/intolerant (R/I) and nilotinib (NI) resistant (R) chronic myelogenous leukemia (CML).

Reporting group title	AP-CML Total (Part 2)

Reporting group description:

All participants who received bosutinib 500 mg orally once daily in advanced phase (AP) chronic myelogenous leukemia (CML) who were imatinib (IM) resistant/intolerant (R/I) or Multi-TKI (multiple tyrosine kinase inhibitor: imatinib, dasatinib and/or nilotinib) resistant/intolerant (R/I).

Reporting group title	BP-CML Total (Part 2)

Reporting group description:

All participants who received bosutinib 500 mg orally once daily in blast phase (BP) chronic

myelogenous leukemia (CML) who were imatinib (IM) resistant/intolerant (R/I) or Multi-TKI (multiple tyrosine kinase inhibitor: imatinib, dasatinib and/or nilotinib) resistant/intolerant (R/I).

Reporting group title	Bosutinib 500 mg, Ph+ ALL (Part 2)

Reporting group description:

Bosutinib 500 mg was administered orally once-daily in participants with philadelphia chromosome-positive acute lymphocytic leukemia (Ph+ ALL)

Serious adverse events	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Total subjects affected by serious adverse events			
subjects affected / exposed	34 / 89 (38.20%)	81 / 195 (41.54%)	15 / 38 (39.47%)
number of deaths (all causes)	2	8	2
number of deaths resulting from adverse events	1	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Blast cell crisis			
subjects affected / exposed	1 / 89 (1.12%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Blast crisis in myelogenous leukaemia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	1 / 89 (1.12%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chloroma			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic myelomonocytic leukaemia			

subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer metastatic			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Keratoacanthoma			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukaemia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melanocytic naevus			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm skin			

subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-small cell lung cancer			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 89 (1.12%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid neoplasm			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine Leiomyoma			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bowen's disease			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angiomyolipoma			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anogenital warts			

subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central nervous system leukaemia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Laryngeal neoplasm			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm prostate			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraproteinaemia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 89 (0.00%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic stenosis			

subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrosis ischaemic			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Allogenic bone marrow transplantation therapy			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Knee arthroplasty			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 89 (2.25%)	5 / 195 (2.56%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	1 / 2	4 / 11	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 89 (1.12%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General physical health deterioration			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	1 / 89 (1.12%)	3 / 195 (1.54%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	0 / 89 (0.00%)	3 / 195 (1.54%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 1
Chills			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi-organ failure			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adverse drug reaction			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Local swelling			

subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Submandibular mass			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adhesion			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			

subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Pregnancy of partner			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Breast hyperplasia			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical dysplasia			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysfunctional uterine bleeding			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic pain			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal haemorrhage			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Menorrhagia			
subjects affected / exposed	0 / 89 (0.00%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	4 / 89 (4.49%)	8 / 195 (4.10%)	3 / 38 (7.89%)
occurrences causally related to treatment / all	0 / 7	2 / 9	1 / 3
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 89 (1.12%)	5 / 195 (2.56%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 10	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 89 (0.00%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	1 / 89 (1.12%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lung infiltration			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Organising pneumonia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Haemoptysis			

subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hallucination, visual			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status change			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 89 (0.00%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase			

increased			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood glucose increased			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood pressure increased			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin decreased			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test abnormal			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			

subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraocular pressure increased			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Abdominal injury			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical vertebral fracture			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal stoma complication			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			

subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematuria			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural swelling			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seroma			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haemorrhage			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth fracture			

subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transfusion reaction			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound haematoma			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bone fracture			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to anastomose			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle injury			

subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural haemorrhage			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Cytogenetic abnormality			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 89 (0.00%)	3 / 195 (1.54%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 89 (0.00%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 89 (1.12%)	3 / 195 (1.54%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac failure congestive			
subjects affected / exposed	2 / 89 (2.25%)	3 / 195 (1.54%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 3	0 / 6	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0

Coronary artery disease			
subjects affected / exposed	1 / 89 (1.12%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	1 / 89 (1.12%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	2 / 89 (2.25%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 89 (0.00%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular dysfunction			
subjects affected / exposed	0 / 89 (0.00%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial haemorrhage			

subjects affected / exposed	0 / 89 (0.00%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiorenal syndrome			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extrasystoles			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuropericarditis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			

subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorder			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 89 (1.12%)	3 / 195 (1.54%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid arteriosclerosis			

subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis post varicella			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraventricular haemorrhage			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoparesis			

subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Speech disorder			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebellar infarction			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinson's disease			

subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculitis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Trigeminal neuralgia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 89 (0.00%)	3 / 195 (1.54%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	4 / 5	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 89 (0.00%)	3 / 195 (1.54%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	3 / 38 (7.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Granulocytopenia			

subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenomegaly			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukostasis syndrome			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glaucoma			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual acuity reduced			

subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitreous haemorrhage			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 89 (3.37%)	4 / 195 (2.05%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	2 / 3	3 / 5	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	2 / 89 (2.25%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 89 (1.12%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	2 / 89 (2.25%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			

subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	1 / 89 (1.12%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toothache			
subjects affected / exposed	2 / 89 (2.25%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal adhesions			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal distension			

subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dental caries			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epigastric discomfort			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			

subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis erosive			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 89 (1.12%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctitis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal haemorrhage			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain lower			

subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal stenosis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			

subjects affected / exposed	0 / 89 (0.00%)	3 / 195 (1.54%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stone			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder disorder			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perforation bile duct			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	6 / 89 (6.74%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	4 / 6	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angioedema			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Circumoral oedema			

subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema multiforme			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin lesion			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash generalised			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 89 (0.00%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute prerenal failure			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus bladder			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis haemorrhagic			

subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	1 / 89 (1.12%)	4 / 195 (2.05%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Chronic kidney disease			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prerenal failure			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal disorder			

subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 89 (2.25%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone cyst			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin pain			

subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myositis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteochondrosis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal column stenosis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			

subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	5 / 89 (5.62%)	6 / 195 (3.08%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 7	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sepsis			
subjects affected / exposed	0 / 89 (0.00%)	3 / 195 (1.54%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 89 (0.00%)	3 / 195 (1.54%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			

subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 89 (1.12%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 89 (1.12%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 89 (0.00%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	1 / 89 (1.12%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			

subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain abscess			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 89 (0.00%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal sepsis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			

subjects affected / exposed	0 / 89 (0.00%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal infection			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 89 (1.12%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gingival abscess			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	2 / 89 (2.25%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			

subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchitis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia fungal			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia necrotising			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomembranous colitis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal sepsis			

subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 89 (0.00%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth abscess			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth infection			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 89 (1.12%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneunomia			

subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious colitis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal abscess			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedure infection			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary mycosis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acidosis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 89 (0.00%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid retention			

subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	19 / 50 (38.00%)	5 / 26 (19.23%)
number of deaths (all causes)	0	3	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Blast cell crisis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blast crisis in myelogenous leukaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chloroma			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic myelomonocytic leukaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer metastatic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Keratoacanthoma			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melanocytic naevus			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm skin			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-small cell lung cancer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid neoplasm			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine Leiomyoma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bowen's disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angiomyolipoma			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anogenital warts			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central nervous system leukaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal neoplasm			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm prostate			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraproteinaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic stenosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrosis ischaemic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Allogenic bone marrow transplantation therapy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Knee arthroplasty			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi-organ failure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adverse drug reaction			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Local swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Submandibular mass			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adhesion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Drug hypersensitivity			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Pregnancy of partner			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Breast hyperplasia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical dysplasia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysfunctional uterine bleeding			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Menorrhagia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	3 / 50 (6.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	2 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	2 / 50 (4.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dyspnoea exertional			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infiltration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organising pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			

subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination, visual			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status change			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood glucose increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood pressure increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test abnormal			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraocular pressure increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Abdominal injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical vertebral fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal stoma complication			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seroma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haemorrhage			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transfusion reaction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound haematoma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bone fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to anastomose			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Cytogenetic abnormality			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 5 (0.00%)	2 / 50 (4.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac failure congestive			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 5 (0.00%)	2 / 50 (4.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular dysfunction			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiorenal syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extrasystoles			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuropericarditis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid arteriosclerosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis post varicella			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraventricular haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoparesis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Speech disorder			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebellar infarction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinson's disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Trigeminal neuralgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			

subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Granulocytopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenomegaly			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukostasis syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glaucoma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual acuity reduced			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitreous haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			

subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toothache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal adhesions			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal distension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dental caries			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epigastric discomfort			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis erosive			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Melaena			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal haemorrhage			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain lower			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal stenosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stone			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perforation bile duct			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angioedema			

subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Circumoral oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema multiforme			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin lesion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash generalised			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute prerenal failure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus bladder			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis haemorrhagic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prerenal failure			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 5 (0.00%)	2 / 50 (4.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone cyst			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myositis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteochondrosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal column stenosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain abscess			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal sepsis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gingival abscess			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia fungal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia necrotising			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomembranous colitis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal sepsis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth abscess			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneunomia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious colitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal abscess			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedure infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary mycosis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acidosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid retention			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	AP-CML Total (Part 2)	BP-CML Total (Part 2)	Bosutinib 500 mg, Ph+ ALL (Part 2)
Total subjects affected by serious adverse events			
subjects affected / exposed	43 / 79 (54.43%)	37 / 64 (57.81%)	17 / 24 (70.83%)
number of deaths (all causes)	11	13	8
number of deaths resulting from adverse events	2	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Blast cell crisis			
subjects affected / exposed	1 / 79 (1.27%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blast crisis in myelogenous leukaemia			
subjects affected / exposed	1 / 79 (1.27%)	2 / 64 (3.13%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			

subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chloroma			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic myelomonocytic leukaemia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer metastatic			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Keratoacanthoma			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukaemia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			

subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melanocytic naevus			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm skin			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-small cell lung cancer			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid neoplasm			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine Leiomyoma			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bowen's disease			

subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angiomyolipoma			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anogenital warts			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central nervous system leukaemia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic myeloid leukaemia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Laryngeal neoplasm			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm prostate			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraproteinaemia			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			

subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	1 / 79 (1.27%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic stenosis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrosis ischaemic			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Allogenic bone marrow transplantation therapy			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Knee arthroplasty			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	4 / 79 (5.06%)	5 / 64 (7.81%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	2 / 5	1 / 10	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	3 / 79 (3.80%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 79 (1.27%)	3 / 64 (4.69%)	2 / 24 (8.33%)
occurrences causally related to treatment / all	0 / 2	1 / 4	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 1
Asthenia			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	4 / 79 (5.06%)	3 / 64 (4.69%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 6	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 4	0 / 3	0 / 1
Chills			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi-organ failure			
subjects affected / exposed	2 / 79 (2.53%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Oedema			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			

subjects affected / exposed	0 / 79 (0.00%)	2 / 64 (3.13%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adverse drug reaction			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Local swelling			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Submandibular mass			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adhesion			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			

subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Pregnancy of partner			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Breast hyperplasia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical dysplasia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysfunctional uterine bleeding			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic pain			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vaginal haemorrhage			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Menorrhagia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	5 / 79 (6.33%)	2 / 64 (3.13%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	7 / 7	2 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	4 / 79 (5.06%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 5	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 79 (1.27%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 79 (1.27%)	2 / 64 (3.13%)	2 / 24 (8.33%)
occurrences causally related to treatment / all	1 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	1 / 1	0 / 2	0 / 1
Asthma			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infiltration			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organising pneumonia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			

subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination, visual			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status change			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

Platelet count decreased			
subjects affected / exposed	2 / 79 (2.53%)	0 / 64 (0.00%)	2 / 24 (8.33%)
occurrences causally related to treatment / all	13 / 17	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood glucose increased			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood pressure increased			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin decreased			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			

subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test abnormal			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraocular pressure increased			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Abdominal injury			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical vertebral fracture			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal stoma complication			

subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematuria			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural swelling			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seroma			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			

subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haemorrhage			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth fracture			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transfusion reaction			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound haematoma			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bone fracture			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to anastomose			

subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle injury			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural haemorrhage			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular pseudoaneurysm			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Cytogenetic abnormality			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	1 / 79 (1.27%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0

Cardiac failure			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	2 / 79 (2.53%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			

subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Left ventricular dysfunction			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial haemorrhage			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	2 / 79 (2.53%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiorenal syndrome			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extrasystoles			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			

subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuropericarditis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorder			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 79 (5.06%)	2 / 64 (3.13%)	2 / 24 (8.33%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 79 (1.27%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hemiparesis			

subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid arteriosclerosis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cerebrovascular accident			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Dizziness			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis post varicella			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraventricular haemorrhage			

subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Loss of consciousness			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoparesis			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Speech disorder			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebellar infarction			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			
subjects affected / exposed	0 / 79 (0.00%)	2 / 64 (3.13%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinson's disease			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Trigeminal neuralgia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	3 / 79 (3.80%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	5 / 79 (6.33%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	1 / 79 (1.27%)	3 / 64 (4.69%)	4 / 24 (16.67%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			

subjects affected / exposed	1 / 79 (1.27%)	2 / 64 (3.13%)	2 / 24 (8.33%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Granulocytopenia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenomegaly			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukostasis syndrome			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Eye disorders			
Diplopia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glaucoma			

subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual acuity reduced			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitreous haemorrhage			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 79 (1.27%)	1 / 64 (1.56%)	2 / 24 (8.33%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 79 (0.00%)	5 / 64 (7.81%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	2 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 79 (0.00%)	2 / 64 (3.13%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 79 (0.00%)	4 / 64 (6.25%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	3 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			

subjects affected / exposed	3 / 79 (3.80%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 5	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toothache			

subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal adhesions			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal distension			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dental caries			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			

subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epigastric discomfort			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis erosive			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctitis			

subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal haemorrhage			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain lower			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal stenosis			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	1 / 79 (1.27%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stone			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder disorder			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perforation bile duct			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			

subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angioedema			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Circumoral oedema			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema multiforme			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin lesion			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash generalised			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute prerenal failure			

subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus bladder			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis haemorrhagic			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 79 (0.00%)	2 / 64 (3.13%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			

subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prerenal failure			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal disorder			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			

subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone cyst			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin pain			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myositis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteochondrosis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal column stenosis			

subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	9 / 79 (11.39%)	5 / 64 (7.81%)	3 / 24 (12.50%)
occurrences causally related to treatment / all	2 / 12	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 1	1 / 2
Sepsis			

subjects affected / exposed	4 / 79 (5.06%)	1 / 64 (1.56%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	1 / 5	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Urinary tract infection			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 79 (0.00%)	2 / 64 (3.13%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Septic shock			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			

subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Abscess limb			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain abscess			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			

subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal sepsis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal infection			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gingival abscess			

subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia fungal			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia necrotising			

subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomembranous colitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal sepsis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth abscess			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth infection			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection bacterial			

subjects affected / exposed	1 / 79 (1.27%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneunomia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious colitis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal abscess			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedure infection			

subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary mycosis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 79 (1.27%)	1 / 64 (1.56%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 79 (0.00%)	3 / 64 (4.69%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Acidosis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			

subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid retention			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Bosutinib 500 mg, CP2L-CML IM-I (Part 2)	Bosutinib 500 mg, CP2L-CML IM-R (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-R (Part 2)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	89 / 89 (100.00%)	194 / 195 (99.49%)	38 / 38 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 89 (6.74%)	17 / 195 (8.72%)	2 / 38 (5.26%)
occurrences (all)	14	32	2
Flushing			
subjects affected / exposed	2 / 89 (2.25%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences (all)	2	1	0
Haematoma			
subjects affected / exposed	2 / 89 (2.25%)	3 / 195 (1.54%)	0 / 38 (0.00%)
occurrences (all)	3	3	0
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	17 / 89 (19.10%)	58 / 195 (29.74%)	5 / 38 (13.16%)
occurrences (all)	25	111	5
Fatigue			
subjects affected / exposed	24 / 89 (26.97%)	49 / 195 (25.13%)	8 / 38 (21.05%)
occurrences (all)	66	111	8
Asthenia			
subjects affected / exposed	16 / 89 (17.98%)	25 / 195 (12.82%)	2 / 38 (5.26%)
occurrences (all)	36	81	2
Oedema peripheral			
subjects affected / exposed	11 / 89 (12.36%)	17 / 195 (8.72%)	1 / 38 (2.63%)
occurrences (all)	16	25	1
Pain			
subjects affected / exposed	5 / 89 (5.62%)	16 / 195 (8.21%)	2 / 38 (5.26%)
occurrences (all)	14	19	11
Chest pain			
subjects affected / exposed	7 / 89 (7.87%)	13 / 195 (6.67%)	1 / 38 (2.63%)
occurrences (all)	10	18	1
Oedema			
subjects affected / exposed	4 / 89 (4.49%)	9 / 195 (4.62%)	2 / 38 (5.26%)
occurrences (all)	5	9	8
Chills			
subjects affected / exposed	5 / 89 (5.62%)	13 / 195 (6.67%)	0 / 38 (0.00%)
occurrences (all)	5	15	0
Chest discomfort			
subjects affected / exposed	2 / 89 (2.25%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences (all)	3	1	0
Face oedema			
subjects affected / exposed	2 / 89 (2.25%)	4 / 195 (2.05%)	0 / 38 (0.00%)
occurrences (all)	2	4	0
Influenza like illness			
subjects affected / exposed	5 / 89 (5.62%)	6 / 195 (3.08%)	1 / 38 (2.63%)
occurrences (all)	6	6	2
Temperature intolerance			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0

Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	3 / 38 (7.89%)
occurrences (all)	0	2	7
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	19 / 89 (21.35%)	46 / 195 (23.59%)	7 / 38 (18.42%)
occurrences (all)	24	67	7
Dyspnoea			
subjects affected / exposed	9 / 89 (10.11%)	23 / 195 (11.79%)	2 / 38 (5.26%)
occurrences (all)	11	33	3
Oropharyngeal pain			
subjects affected / exposed	10 / 89 (11.24%)	25 / 195 (12.82%)	2 / 38 (5.26%)
occurrences (all)	12	28	3
Pleural effusion			
subjects affected / exposed	7 / 89 (7.87%)	18 / 195 (9.23%)	3 / 38 (7.89%)
occurrences (all)	14	25	12
Dyspnoea exertional			
subjects affected / exposed	1 / 89 (1.12%)	7 / 195 (3.59%)	1 / 38 (2.63%)
occurrences (all)	1	9	1
Epistaxis			
subjects affected / exposed	1 / 89 (1.12%)	3 / 195 (1.54%)	1 / 38 (2.63%)
occurrences (all)	1	4	1
Atelectasis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	2 / 89 (2.25%)	4 / 195 (2.05%)	0 / 38 (0.00%)
occurrences (all)	2	4	0
Pulmonary hilum mass			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Pulmonary mass			

subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
Rales			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	2 / 89 (2.25%)	4 / 195 (2.05%)	0 / 38 (0.00%)
occurrences (all)	2	4	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 89 (3.37%)	6 / 195 (3.08%)	1 / 38 (2.63%)
occurrences (all)	3	7	2
Anxiety			
subjects affected / exposed	7 / 89 (7.87%)	8 / 195 (4.10%)	1 / 38 (2.63%)
occurrences (all)	7	11	1
Depression			
subjects affected / exposed	4 / 89 (4.49%)	9 / 195 (4.62%)	0 / 38 (0.00%)
occurrences (all)	4	11	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	21 / 89 (23.60%)	42 / 195 (21.54%)	6 / 38 (15.79%)
occurrences (all)	54	107	9
Platelet count decreased			
subjects affected / exposed	11 / 89 (12.36%)	16 / 195 (8.21%)	1 / 38 (2.63%)
occurrences (all)	50	53	2
Weight decreased			
subjects affected / exposed	8 / 89 (8.99%)	27 / 195 (13.85%)	0 / 38 (0.00%)
occurrences (all)	12	29	0
Blood creatinine increased			
subjects affected / exposed	8 / 89 (8.99%)	18 / 195 (9.23%)	4 / 38 (10.53%)
occurrences (all)	19	27	5
Lipase increased			
subjects affected / exposed	9 / 89 (10.11%)	17 / 195 (8.72%)	3 / 38 (7.89%)
occurrences (all)	16	29	3
Blood alkaline phosphatase increased			

subjects affected / exposed	3 / 89 (3.37%)	6 / 195 (3.08%)	3 / 38 (7.89%)
occurrences (all)	5	7	5
Amylase increased			
subjects affected / exposed	3 / 89 (3.37%)	12 / 195 (6.15%)	2 / 38 (5.26%)
occurrences (all)	7	15	2
Aspartate aminotransferase increased			
subjects affected / exposed	18 / 89 (20.22%)	38 / 195 (19.49%)	2 / 38 (5.26%)
occurrences (all)	39	81	2
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 89 (1.12%)	14 / 195 (7.18%)	1 / 38 (2.63%)
occurrences (all)	1	24	2
Haemoglobin decreased			
subjects affected / exposed	10 / 89 (11.24%)	6 / 195 (3.08%)	1 / 38 (2.63%)
occurrences (all)	23	11	3
Weight increased			
subjects affected / exposed	3 / 89 (3.37%)	12 / 195 (6.15%)	3 / 38 (7.89%)
occurrences (all)	5	18	4
White blood cell count decreased			
subjects affected / exposed	9 / 89 (10.11%)	6 / 195 (3.08%)	0 / 38 (0.00%)
occurrences (all)	25	9	0
Blood urea increased			
subjects affected / exposed	1 / 89 (1.12%)	3 / 195 (1.54%)	2 / 38 (5.26%)
occurrences (all)	1	3	2
Blood uric acid increased			
subjects affected / exposed	1 / 89 (1.12%)	11 / 195 (5.64%)	2 / 38 (5.26%)
occurrences (all)	1	13	2
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 89 (2.25%)	4 / 195 (2.05%)	3 / 38 (7.89%)
occurrences (all)	2	6	3
Globulins decreased			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences (all)	0	0	2
Haematocrit decreased			

subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	5 / 89 (5.62%)	3 / 195 (1.54%)	0 / 38 (0.00%)
occurrences (all)	15	10	0
White blood cells urine positive			
subjects affected / exposed	0 / 89 (0.00%)	3 / 195 (1.54%)	0 / 38 (0.00%)
occurrences (all)	0	4	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	7 / 89 (7.87%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences (all)	9	1	0
Procedural pain			
subjects affected / exposed	2 / 89 (2.25%)	5 / 195 (2.56%)	0 / 38 (0.00%)
occurrences (all)	4	5	0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	2 / 89 (2.25%)	3 / 195 (1.54%)	1 / 38 (2.63%)
occurrences (all)	2	6	1
Mitral valve incompetence			
subjects affected / exposed	1 / 89 (1.12%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences (all)	1	1	0
Tachycardia			
subjects affected / exposed	0 / 89 (0.00%)	3 / 195 (1.54%)	0 / 38 (0.00%)
occurrences (all)	0	3	0
Nervous system disorders			
Headache			
subjects affected / exposed	18 / 89 (20.22%)	35 / 195 (17.95%)	7 / 38 (18.42%)
occurrences (all)	50	88	13
Dizziness			
subjects affected / exposed	9 / 89 (10.11%)	16 / 195 (8.21%)	5 / 38 (13.16%)
occurrences (all)	17	23	5
Hypoaesthesia			
subjects affected / exposed	2 / 89 (2.25%)	11 / 195 (5.64%)	0 / 38 (0.00%)
occurrences (all)	2	19	0
Paraesthesia			

subjects affected / exposed	3 / 89 (3.37%)	11 / 195 (5.64%)	0 / 38 (0.00%)
occurrences (all)	4	11	0
Dysgeusia			
subjects affected / exposed	2 / 89 (2.25%)	3 / 195 (1.54%)	0 / 38 (0.00%)
occurrences (all)	3	3	0
Neuropathy peripheral			
subjects affected / exposed	1 / 89 (1.12%)	3 / 195 (1.54%)	0 / 38 (0.00%)
occurrences (all)	1	4	0
Sensory disturbance			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	2 / 89 (2.25%)	4 / 195 (2.05%)	0 / 38 (0.00%)
occurrences (all)	4	4	0
Syncope			
subjects affected / exposed	1 / 89 (1.12%)	3 / 195 (1.54%)	0 / 38 (0.00%)
occurrences (all)	1	3	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	32 / 89 (35.96%)	61 / 195 (31.28%)	9 / 38 (23.68%)
occurrences (all)	155	278	35
Anaemia			
subjects affected / exposed	24 / 89 (26.97%)	45 / 195 (23.08%)	7 / 38 (18.42%)
occurrences (all)	55	162	14
Neutropenia			
subjects affected / exposed	13 / 89 (14.61%)	26 / 195 (13.33%)	8 / 38 (21.05%)
occurrences (all)	52	72	25
Leukopenia			
subjects affected / exposed	8 / 89 (8.99%)	19 / 195 (9.74%)	4 / 38 (10.53%)
occurrences (all)	35	35	13
Leukocytosis			
subjects affected / exposed	0 / 89 (0.00%)	7 / 195 (3.59%)	1 / 38 (2.63%)
occurrences (all)	0	10	1
Ear and labyrinth disorders			
Ear pain			

subjects affected / exposed	2 / 89 (2.25%)	3 / 195 (1.54%)	2 / 38 (5.26%)
occurrences (all)	2	4	3
Eye disorders			
Eye oedema			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences (all)	0	1	0
Scleral haemorrhage			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	1 / 89 (1.12%)	3 / 195 (1.54%)	2 / 38 (5.26%)
occurrences (all)	1	3	2
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	76 / 89 (85.39%)	166 / 195 (85.13%)	30 / 38 (78.95%)
occurrences (all)	513	1710	189
Nausea			
subjects affected / exposed	46 / 89 (51.69%)	85 / 195 (43.59%)	20 / 38 (52.63%)
occurrences (all)	98	290	65
Vomiting			
subjects affected / exposed	32 / 89 (35.96%)	73 / 195 (37.44%)	14 / 38 (36.84%)
occurrences (all)	52	237	32
Abdominal pain			
subjects affected / exposed	24 / 89 (26.97%)	50 / 195 (25.64%)	8 / 38 (21.05%)
occurrences (all)	37	121	12
Abdominal pain upper			
subjects affected / exposed	17 / 89 (19.10%)	41 / 195 (21.03%)	8 / 38 (21.05%)
occurrences (all)	34	121	34
Constipation			
subjects affected / exposed	17 / 89 (19.10%)	22 / 195 (11.28%)	2 / 38 (5.26%)
occurrences (all)	29	35	5
Dyspepsia			
subjects affected / exposed	7 / 89 (7.87%)	21 / 195 (10.77%)	7 / 38 (18.42%)
occurrences (all)	14	52	30
Abdominal distension			

subjects affected / exposed	8 / 89 (8.99%)	17 / 195 (8.72%)	2 / 38 (5.26%)
occurrences (all)	11	68	2
Flatulence			
subjects affected / exposed	6 / 89 (6.74%)	4 / 195 (2.05%)	3 / 38 (7.89%)
occurrences (all)	19	11	5
Abdominal discomfort			
subjects affected / exposed	9 / 89 (10.11%)	8 / 195 (4.10%)	1 / 38 (2.63%)
occurrences (all)	18	11	2
Toothache			
subjects affected / exposed	6 / 89 (6.74%)	12 / 195 (6.15%)	2 / 38 (5.26%)
occurrences (all)	9	17	3
Aphthous stomatitis			
subjects affected / exposed	2 / 89 (2.25%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences (all)	2	2	0
Gastrointestinal sounds abnormal			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences (all)	0	0	1
Gingival bleeding			
subjects affected / exposed	1 / 89 (1.12%)	5 / 195 (2.56%)	1 / 38 (2.63%)
occurrences (all)	1	7	4
Gingival pain			
subjects affected / exposed	2 / 89 (2.25%)	2 / 195 (1.03%)	2 / 38 (5.26%)
occurrences (all)	3	3	3
Haemorrhoids			
subjects affected / exposed	2 / 89 (2.25%)	7 / 195 (3.59%)	1 / 38 (2.63%)
occurrences (all)	2	12	2
Mouth ulceration			
subjects affected / exposed	3 / 89 (3.37%)	6 / 195 (3.08%)	0 / 38 (0.00%)
occurrences (all)	3	7	0
Stomatitis			
subjects affected / exposed	0 / 89 (0.00%)	2 / 195 (1.03%)	1 / 38 (2.63%)
occurrences (all)	0	3	3
Tongue oedema			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			

Hyperbilirubinaemia			
subjects affected / exposed	1 / 89 (1.12%)	4 / 195 (2.05%)	0 / 38 (0.00%)
occurrences (all)	2	4	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	36 / 89 (40.45%)	63 / 195 (32.31%)	10 / 38 (26.32%)
occurrences (all)	93	116	14
Pruritus			
subjects affected / exposed	9 / 89 (10.11%)	18 / 195 (9.23%)	9 / 38 (23.68%)
occurrences (all)	17	31	16
Dry skin			
subjects affected / exposed	4 / 89 (4.49%)	16 / 195 (8.21%)	1 / 38 (2.63%)
occurrences (all)	6	23	1
Skin lesion			
subjects affected / exposed	4 / 89 (4.49%)	10 / 195 (5.13%)	2 / 38 (5.26%)
occurrences (all)	4	19	7
Alopecia			
subjects affected / exposed	3 / 89 (3.37%)	11 / 195 (5.64%)	0 / 38 (0.00%)
occurrences (all)	4	14	0
Night sweats			
subjects affected / exposed	1 / 89 (1.12%)	2 / 195 (1.03%)	2 / 38 (5.26%)
occurrences (all)	1	2	2
Angioedema			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 89 (0.00%)	4 / 195 (2.05%)	2 / 38 (5.26%)
occurrences (all)	0	6	4
Ecchymosis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	7 / 89 (7.87%)	5 / 195 (2.56%)	1 / 38 (2.63%)
occurrences (all)	8	6	1
Hyperhidrosis			

subjects affected / exposed	3 / 89 (3.37%)	3 / 195 (1.54%)	1 / 38 (2.63%)
occurrences (all)	4	3	2
Nail disorder			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences (all)	0	0	1
Petechiae			
subjects affected / exposed	0 / 89 (0.00%)	3 / 195 (1.54%)	0 / 38 (0.00%)
occurrences (all)	0	4	0
Skin burning sensation			
subjects affected / exposed	0 / 89 (0.00%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences (all)	0	6	0
Skin depigmentation			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Swelling face			
subjects affected / exposed	1 / 89 (1.12%)	1 / 195 (0.51%)	1 / 38 (2.63%)
occurrences (all)	1	1	1
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	4 / 89 (4.49%)	6 / 195 (3.08%)	3 / 38 (7.89%)
occurrences (all)	4	9	3
Pollakiuria			
subjects affected / exposed	2 / 89 (2.25%)	2 / 195 (1.03%)	0 / 38 (0.00%)
occurrences (all)	2	2	0
Renal failure			
subjects affected / exposed	1 / 89 (1.12%)	3 / 195 (1.54%)	1 / 38 (2.63%)
occurrences (all)	1	4	3
Urinary retention			
subjects affected / exposed	1 / 89 (1.12%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	17 / 89 (19.10%)	31 / 195 (15.90%)	5 / 38 (13.16%)
occurrences (all)	21	40	6
Back pain			

subjects affected / exposed	16 / 89 (17.98%)	22 / 195 (11.28%)	5 / 38 (13.16%)
occurrences (all)	25	31	22
Pain in extremity			
subjects affected / exposed	4 / 89 (4.49%)	27 / 195 (13.85%)	2 / 38 (5.26%)
occurrences (all)	9	45	3
Myalgia			
subjects affected / exposed	7 / 89 (7.87%)	16 / 195 (8.21%)	3 / 38 (7.89%)
occurrences (all)	11	21	3
Bone pain			
subjects affected / exposed	3 / 89 (3.37%)	11 / 195 (5.64%)	3 / 38 (7.89%)
occurrences (all)	4	13	4
Musculoskeletal pain			
subjects affected / exposed	3 / 89 (3.37%)	8 / 195 (4.10%)	5 / 38 (13.16%)
occurrences (all)	3	13	6
Muscle spasms			
subjects affected / exposed	7 / 89 (7.87%)	7 / 195 (3.59%)	2 / 38 (5.26%)
occurrences (all)	14	11	3
Groin pain			
subjects affected / exposed	0 / 89 (0.00%)	1 / 195 (0.51%)	2 / 38 (5.26%)
occurrences (all)	0	2	4
Joint swelling			
subjects affected / exposed	2 / 89 (2.25%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences (all)	2	1	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 89 (1.12%)	2 / 195 (1.03%)	2 / 38 (5.26%)
occurrences (all)	1	3	2
Musculoskeletal stiffness			
subjects affected / exposed	1 / 89 (1.12%)	0 / 195 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
Neck pain			
subjects affected / exposed	2 / 89 (2.25%)	4 / 195 (2.05%)	0 / 38 (0.00%)
occurrences (all)	2	9	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	13 / 89 (14.61%)	25 / 195 (12.82%)	3 / 38 (7.89%)
occurrences (all)	18	34	3

Upper respiratory tract infection			
subjects affected / exposed	9 / 89 (10.11%)	19 / 195 (9.74%)	3 / 38 (7.89%)
occurrences (all)	12	35	8
Influenza			
subjects affected / exposed	6 / 89 (6.74%)	21 / 195 (10.77%)	4 / 38 (10.53%)
occurrences (all)	9	33	7
Urinary tract infection			
subjects affected / exposed	8 / 89 (8.99%)	20 / 195 (10.26%)	1 / 38 (2.63%)
occurrences (all)	15	32	1
Bronchitis			
subjects affected / exposed	3 / 89 (3.37%)	13 / 195 (6.67%)	1 / 38 (2.63%)
occurrences (all)	3	14	1
Sinusitis			
subjects affected / exposed	3 / 89 (3.37%)	7 / 195 (3.59%)	2 / 38 (5.26%)
occurrences (all)	3	7	2
Gastrointestinal infection			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	2 / 38 (5.26%)
occurrences (all)	0	0	5
Gingivitis			
subjects affected / exposed	2 / 89 (2.25%)	4 / 195 (2.05%)	0 / 38 (0.00%)
occurrences (all)	3	5	0
Lower respiratory tract infection			
subjects affected / exposed	1 / 89 (1.12%)	1 / 195 (0.51%)	1 / 38 (2.63%)
occurrences (all)	1	1	1
Oral candidiasis			
subjects affected / exposed	2 / 89 (2.25%)	1 / 195 (0.51%)	0 / 38 (0.00%)
occurrences (all)	2	1	0
Oral herpes			
subjects affected / exposed	3 / 89 (3.37%)	3 / 195 (1.54%)	1 / 38 (2.63%)
occurrences (all)	3	3	1
Pharyngitis			
subjects affected / exposed	5 / 89 (5.62%)	6 / 195 (3.08%)	2 / 38 (5.26%)
occurrences (all)	5	6	3
Pneumonia			
subjects affected / exposed	2 / 89 (2.25%)	2 / 195 (1.03%)	1 / 38 (2.63%)
occurrences (all)	2	2	1

Respiratory tract infection viral			
subjects affected / exposed	3 / 89 (3.37%)	4 / 195 (2.05%)	0 / 38 (0.00%)
occurrences (all)	6	5	0
Wound infection			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	12 / 89 (13.48%)	29 / 195 (14.87%)	3 / 38 (7.89%)
occurrences (all)	16	45	6
Hypokalaemia			
subjects affected / exposed	5 / 89 (5.62%)	10 / 195 (5.13%)	0 / 38 (0.00%)
occurrences (all)	7	15	0
Hypophosphataemia			
subjects affected / exposed	0 / 89 (0.00%)	12 / 195 (6.15%)	0 / 38 (0.00%)
occurrences (all)	0	22	0
Hyperuricaemia			
subjects affected / exposed	6 / 89 (6.74%)	6 / 195 (3.08%)	1 / 38 (2.63%)
occurrences (all)	15	9	2
Hypocalcaemia			
subjects affected / exposed	0 / 89 (0.00%)	8 / 195 (4.10%)	0 / 38 (0.00%)
occurrences (all)	0	9	0
Hyperglycaemia			
subjects affected / exposed	2 / 89 (2.25%)	8 / 195 (4.10%)	2 / 38 (5.26%)
occurrences (all)	3	11	2
Hyperkalaemia			
subjects affected / exposed	2 / 89 (2.25%)	6 / 195 (3.08%)	0 / 38 (0.00%)
occurrences (all)	3	16	0
Hypernatraemia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 195 (0.00%)	2 / 38 (5.26%)
occurrences (all)	0	0	3
Hypoglycaemia			
subjects affected / exposed	1 / 89 (1.12%)	2 / 195 (1.03%)	2 / 38 (5.26%)
occurrences (all)	1	2	2
Hypomagnesaemia			

subjects affected / exposed	1 / 89 (1.12%)	3 / 195 (1.54%)	1 / 38 (2.63%)
occurrences (all)	1	3	1

Non-serious adverse events	Bosutinib 500 mg, CP3L-CML IM R/I, (D+NI) R/I or NI-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + D-I (Part 2)	Bosutinib 500 mg, CP3L-CML IM R/I + NI-R (Part 2)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	50 / 50 (100.00%)	26 / 26 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	5 / 50 (10.00%)	1 / 26 (3.85%)
occurrences (all)	0	7	1
Flushing			
subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Haematoma			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 5 (20.00%)	7 / 50 (14.00%)	3 / 26 (11.54%)
occurrences (all)	1	7	16
Fatigue			
subjects affected / exposed	3 / 5 (60.00%)	12 / 50 (24.00%)	2 / 26 (7.69%)
occurrences (all)	5	22	2
Asthenia			
subjects affected / exposed	2 / 5 (40.00%)	1 / 50 (2.00%)	4 / 26 (15.38%)
occurrences (all)	2	1	10
Oedema peripheral			
subjects affected / exposed	1 / 5 (20.00%)	4 / 50 (8.00%)	4 / 26 (15.38%)
occurrences (all)	1	7	5
Pain			
subjects affected / exposed	2 / 5 (40.00%)	2 / 50 (4.00%)	1 / 26 (3.85%)
occurrences (all)	2	2	1
Chest pain			
subjects affected / exposed	1 / 5 (20.00%)	2 / 50 (4.00%)	0 / 26 (0.00%)
occurrences (all)	1	3	0

Oedema			
subjects affected / exposed	0 / 5 (0.00%)	2 / 50 (4.00%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Chills			
subjects affected / exposed	0 / 5 (0.00%)	3 / 50 (6.00%)	0 / 26 (0.00%)
occurrences (all)	0	3	0
Chest discomfort			
subjects affected / exposed	0 / 5 (0.00%)	2 / 50 (4.00%)	1 / 26 (3.85%)
occurrences (all)	0	2	1
Face oedema			
subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	1 / 26 (3.85%)
occurrences (all)	3	0	1
Influenza like illness			
subjects affected / exposed	1 / 5 (20.00%)	3 / 50 (6.00%)	0 / 26 (0.00%)
occurrences (all)	1	5	0
Temperature intolerance			
subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	1 / 26 (3.85%)
occurrences (all)	0	1	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 5 (40.00%)	12 / 50 (24.00%)	4 / 26 (15.38%)
occurrences (all)	2	17	14
Dyspnoea			
subjects affected / exposed	1 / 5 (20.00%)	9 / 50 (18.00%)	1 / 26 (3.85%)
occurrences (all)	3	23	9
Oropharyngeal pain			
subjects affected / exposed	1 / 5 (20.00%)	3 / 50 (6.00%)	2 / 26 (7.69%)
occurrences (all)	2	5	6
Pleural effusion			
subjects affected / exposed	1 / 5 (20.00%)	13 / 50 (26.00%)	1 / 26 (3.85%)
occurrences (all)	5	27	3
Dyspnoea exertional			

subjects affected / exposed	1 / 5 (20.00%)	5 / 50 (10.00%)	0 / 26 (0.00%)
occurrences (all)	1	5	0
Epistaxis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Atelectasis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 5 (0.00%)	3 / 50 (6.00%)	0 / 26 (0.00%)
occurrences (all)	0	3	0
Productive cough			
subjects affected / exposed	0 / 5 (0.00%)	5 / 50 (10.00%)	0 / 26 (0.00%)
occurrences (all)	0	5	0
Pulmonary hilum mass			
subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Pulmonary mass			
subjects affected / exposed	0 / 5 (0.00%)	3 / 50 (6.00%)	0 / 26 (0.00%)
occurrences (all)	0	3	0
Rales			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	1 / 5 (20.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 5 (60.00%)	5 / 50 (10.00%)	1 / 26 (3.85%)
occurrences (all)	4	6	2
Anxiety			
subjects affected / exposed	0 / 5 (0.00%)	2 / 50 (4.00%)	1 / 26 (3.85%)
occurrences (all)	0	2	7
Depression			
subjects affected / exposed	1 / 5 (20.00%)	3 / 50 (6.00%)	2 / 26 (7.69%)
occurrences (all)	1	3	2

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 5 (20.00%)	6 / 50 (12.00%)	5 / 26 (19.23%)
occurrences (all)	1	15	17
Platelet count decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	2 / 26 (7.69%)
occurrences (all)	0	8	3
Weight decreased			
subjects affected / exposed	0 / 5 (0.00%)	7 / 50 (14.00%)	0 / 26 (0.00%)
occurrences (all)	0	7	0
Blood creatinine increased			
subjects affected / exposed	1 / 5 (20.00%)	6 / 50 (12.00%)	4 / 26 (15.38%)
occurrences (all)	1	11	4
Lipase increased			
subjects affected / exposed	0 / 5 (0.00%)	2 / 50 (4.00%)	2 / 26 (7.69%)
occurrences (all)	0	8	5
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	3 / 26 (11.54%)
occurrences (all)	0	0	3
Amylase increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	3 / 26 (11.54%)
occurrences (all)	0	1	4
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	3 / 50 (6.00%)	4 / 26 (15.38%)
occurrences (all)	0	5	6
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	12
Haemoglobin decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	3 / 26 (11.54%)
occurrences (all)	0	0	3
Weight increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	0	4	0
White blood cell count decreased			

subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	0 / 5 (0.00%)	2 / 50 (4.00%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Blood uric acid increased			
subjects affected / exposed	0 / 5 (0.00%)	2 / 50 (4.00%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	3
Globulins decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Haematocrit decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Neutrophil count decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	0	4	0
White blood cells urine positive			
subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 5 (0.00%)	2 / 50 (4.00%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Procedural pain			
subjects affected / exposed	1 / 5 (20.00%)	2 / 50 (4.00%)	0 / 26 (0.00%)
occurrences (all)	1	2	0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 5 (20.00%)	4 / 50 (8.00%)	0 / 26 (0.00%)
occurrences (all)	1	7	0
Mitral valve incompetence			

subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 5 (20.00%)	15 / 50 (30.00%)	8 / 26 (30.77%)
occurrences (all)	1	26	15
Dizziness			
subjects affected / exposed	2 / 5 (40.00%)	8 / 50 (16.00%)	3 / 26 (11.54%)
occurrences (all)	5	11	5
Hypoaesthesia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Paraesthesia			
subjects affected / exposed	1 / 5 (20.00%)	3 / 50 (6.00%)	0 / 26 (0.00%)
occurrences (all)	1	4	0
Dysgeusia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 50 (2.00%)	1 / 26 (3.85%)
occurrences (all)	1	1	1
Neuropathy peripheral			
subjects affected / exposed	1 / 5 (20.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	1	1	0
Sensory disturbance			
subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Syncope			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Thrombocytopenia			

subjects affected / exposed	3 / 5 (60.00%)	18 / 50 (36.00%)	12 / 26 (46.15%)
occurrences (all)	4	92	44
Anaemia			
subjects affected / exposed	2 / 5 (40.00%)	7 / 50 (14.00%)	6 / 26 (23.08%)
occurrences (all)	2	17	11
Neutropenia			
subjects affected / exposed	1 / 5 (20.00%)	6 / 50 (12.00%)	7 / 26 (26.92%)
occurrences (all)	4	22	12
Leukopenia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Leukocytosis			
subjects affected / exposed	0 / 5 (0.00%)	2 / 50 (4.00%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Eye disorders			
Eye oedema			
subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Scleral haemorrhage			
subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 5 (100.00%)	42 / 50 (84.00%)	22 / 26 (84.62%)
occurrences (all)	10	209	280
Nausea			
subjects affected / exposed	2 / 5 (40.00%)	23 / 50 (46.00%)	12 / 26 (46.15%)
occurrences (all)	2	42	39
Vomiting			

subjects affected / exposed	0 / 5 (0.00%)	24 / 50 (48.00%)	7 / 26 (26.92%)
occurrences (all)	0	40	16
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	12 / 50 (24.00%)	8 / 26 (30.77%)
occurrences (all)	0	20	37
Abdominal pain upper			
subjects affected / exposed	0 / 5 (0.00%)	9 / 50 (18.00%)	4 / 26 (15.38%)
occurrences (all)	0	44	17
Constipation			
subjects affected / exposed	2 / 5 (40.00%)	7 / 50 (14.00%)	3 / 26 (11.54%)
occurrences (all)	2	11	8
Dyspepsia			
subjects affected / exposed	0 / 5 (0.00%)	4 / 50 (8.00%)	1 / 26 (3.85%)
occurrences (all)	0	6	1
Abdominal distension			
subjects affected / exposed	0 / 5 (0.00%)	4 / 50 (8.00%)	3 / 26 (11.54%)
occurrences (all)	0	5	11
Flatulence			
subjects affected / exposed	0 / 5 (0.00%)	3 / 50 (6.00%)	1 / 26 (3.85%)
occurrences (all)	0	5	1
Abdominal discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	1 / 5 (20.00%)	2 / 50 (4.00%)	0 / 26 (0.00%)
occurrences (all)	1	3	0
Aphthous stomatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	4
Gastrointestinal sounds abnormal			
subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Gingival bleeding			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Gingival pain			

subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Haemorrhoids			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	3 / 26 (11.54%)
occurrences (all)	0	0	4
Mouth ulceration			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	2 / 26 (7.69%)
occurrences (all)	0	1	4
Stomatitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Tongue oedema			
subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	1	3	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 5 (40.00%)	18 / 50 (36.00%)	3 / 26 (11.54%)
occurrences (all)	5	31	9
Pruritus			
subjects affected / exposed	0 / 5 (0.00%)	8 / 50 (16.00%)	3 / 26 (11.54%)
occurrences (all)	0	9	4
Dry skin			
subjects affected / exposed	0 / 5 (0.00%)	4 / 50 (8.00%)	3 / 26 (11.54%)
occurrences (all)	0	6	4
Skin lesion			
subjects affected / exposed	0 / 5 (0.00%)	2 / 50 (4.00%)	2 / 26 (7.69%)
occurrences (all)	0	2	2
Alopecia			
subjects affected / exposed	1 / 5 (20.00%)	3 / 50 (6.00%)	0 / 26 (0.00%)
occurrences (all)	1	4	0
Night sweats			

subjects affected / exposed	0 / 5 (0.00%)	3 / 50 (6.00%)	1 / 26 (3.85%)
occurrences (all)	0	3	2
Angioedema			
subjects affected / exposed	1 / 5 (20.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	3	4	0
Dermatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	2
Ecchymosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Erythema			
subjects affected / exposed	0 / 5 (0.00%)	2 / 50 (4.00%)	2 / 26 (7.69%)
occurrences (all)	0	2	8
Hyperhidrosis			
subjects affected / exposed	0 / 5 (0.00%)	3 / 50 (6.00%)	1 / 26 (3.85%)
occurrences (all)	0	4	3
Nail disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Petechiae			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Skin burning sensation			
subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Skin depigmentation			
subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	2	0	0
Swelling face			
subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2

Pollakiuria			
subjects affected / exposed	1 / 5 (20.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	2	1	0
Renal failure			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Urinary retention			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	10 / 50 (20.00%)	6 / 26 (23.08%)
occurrences (all)	0	19	23
Back pain			
subjects affected / exposed	1 / 5 (20.00%)	5 / 50 (10.00%)	3 / 26 (11.54%)
occurrences (all)	1	5	5
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	5 / 50 (10.00%)	3 / 26 (11.54%)
occurrences (all)	0	8	12
Myalgia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	1 / 26 (3.85%)
occurrences (all)	0	2	1
Bone pain			
subjects affected / exposed	0 / 5 (0.00%)	5 / 50 (10.00%)	1 / 26 (3.85%)
occurrences (all)	0	7	1
Musculoskeletal pain			
subjects affected / exposed	0 / 5 (0.00%)	3 / 50 (6.00%)	2 / 26 (7.69%)
occurrences (all)	0	4	2
Muscle spasms			
subjects affected / exposed	0 / 5 (0.00%)	5 / 50 (10.00%)	1 / 26 (3.85%)
occurrences (all)	0	5	12
Groin pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Joint swelling			

subjects affected / exposed	1 / 5 (20.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	1	2	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal stiffness			
subjects affected / exposed	1 / 5 (20.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	1	1	0
Neck pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	5
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 5 (20.00%)	5 / 50 (10.00%)	4 / 26 (15.38%)
occurrences (all)	1	5	5
Upper respiratory tract infection			
subjects affected / exposed	2 / 5 (40.00%)	7 / 50 (14.00%)	0 / 26 (0.00%)
occurrences (all)	2	13	0
Influenza			
subjects affected / exposed	1 / 5 (20.00%)	4 / 50 (8.00%)	3 / 26 (11.54%)
occurrences (all)	1	4	3
Urinary tract infection			
subjects affected / exposed	1 / 5 (20.00%)	2 / 50 (4.00%)	2 / 26 (7.69%)
occurrences (all)	1	2	2
Bronchitis			
subjects affected / exposed	1 / 5 (20.00%)	2 / 50 (4.00%)	1 / 26 (3.85%)
occurrences (all)	1	3	2
Sinusitis			
subjects affected / exposed	1 / 5 (20.00%)	4 / 50 (8.00%)	0 / 26 (0.00%)
occurrences (all)	1	5	0
Gastrointestinal infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2

Lower respiratory tract infection			
subjects affected / exposed	1 / 5 (20.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	1	2	0
Oral candidiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	2
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	3 / 50 (6.00%)	1 / 26 (3.85%)
occurrences (all)	0	3	1
Respiratory tract infection viral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 50 (0.00%)	3 / 26 (11.54%)
occurrences (all)	0	0	7
Wound infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 5 (20.00%)	7 / 50 (14.00%)	4 / 26 (15.38%)
occurrences (all)	1	10	5
Hypokalaemia			
subjects affected / exposed	0 / 5 (0.00%)	3 / 50 (6.00%)	2 / 26 (7.69%)
occurrences (all)	0	7	5
Hypophosphataemia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 50 (2.00%)	1 / 26 (3.85%)
occurrences (all)	1	2	2
Hyperuricaemia			
subjects affected / exposed	1 / 5 (20.00%)	5 / 50 (10.00%)	0 / 26 (0.00%)
occurrences (all)	1	7	0
Hypocalcaemia			

subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	0	3	0
Hyperglycaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	2 / 26 (7.69%)
occurrences (all)	0	1	3
Hyperkalaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	4 / 26 (15.38%)
occurrences (all)	0	1	7
Hypernatraemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Hypoglycaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 50 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Hypomagnesaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 50 (2.00%)	0 / 26 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	AP-CML Total (Part 2)	BP-CML Total (Part 2)	Bosutinib 500 mg, Ph+ ALL (Part 2)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	79 / 79 (100.00%)	62 / 64 (96.88%)	23 / 24 (95.83%)
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 79 (7.59%)	2 / 64 (3.13%)	2 / 24 (8.33%)
occurrences (all)	8	2	2
Flushing			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	3 / 24 (12.50%)
occurrences (all)	2	0	3
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	28 / 79 (35.44%)	22 / 64 (34.38%)	10 / 24 (41.67%)
occurrences (all)	44	29	11
Fatigue			

subjects affected / exposed	17 / 79 (21.52%)	13 / 64 (20.31%)	5 / 24 (20.83%)
occurrences (all)	22	16	6
Asthenia			
subjects affected / exposed	11 / 79 (13.92%)	3 / 64 (4.69%)	5 / 24 (20.83%)
occurrences (all)	23	4	7
Oedema peripheral			
subjects affected / exposed	6 / 79 (7.59%)	7 / 64 (10.94%)	5 / 24 (20.83%)
occurrences (all)	13	8	5
Pain			
subjects affected / exposed	6 / 79 (7.59%)	3 / 64 (4.69%)	2 / 24 (8.33%)
occurrences (all)	9	4	3
Chest pain			
subjects affected / exposed	6 / 79 (7.59%)	3 / 64 (4.69%)	2 / 24 (8.33%)
occurrences (all)	8	4	2
Oedema			
subjects affected / exposed	5 / 79 (6.33%)	2 / 64 (3.13%)	2 / 24 (8.33%)
occurrences (all)	5	2	2
Chills			
subjects affected / exposed	3 / 79 (3.80%)	2 / 64 (3.13%)	3 / 24 (12.50%)
occurrences (all)	3	2	3
Chest discomfort			
subjects affected / exposed	4 / 79 (5.06%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	4	2	0
Face oedema			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Influenza like illness			
subjects affected / exposed	1 / 79 (1.27%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	1	1	0
Temperature intolerance			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	24 / 79 (30.38%)	8 / 64 (12.50%)	1 / 24 (4.17%)
occurrences (all)	43	8	1
Dyspnoea			
subjects affected / exposed	14 / 79 (17.72%)	12 / 64 (18.75%)	4 / 24 (16.67%)
occurrences (all)	24	15	4
Oropharyngeal pain			
subjects affected / exposed	8 / 79 (10.13%)	3 / 64 (4.69%)	2 / 24 (8.33%)
occurrences (all)	14	5	2
Pleural effusion			
subjects affected / exposed	8 / 79 (10.13%)	2 / 64 (3.13%)	2 / 24 (8.33%)
occurrences (all)	11	2	3
Dyspnoea exertional			
subjects affected / exposed	3 / 79 (3.80%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	3	1	0
Epistaxis			
subjects affected / exposed	3 / 79 (3.80%)	3 / 64 (4.69%)	2 / 24 (8.33%)
occurrences (all)	7	4	3
Atelectasis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2
Nasal congestion			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Productive cough			
subjects affected / exposed	0 / 79 (0.00%)	2 / 64 (3.13%)	0 / 24 (0.00%)
occurrences (all)	0	4	0
Pulmonary hilum mass			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Pulmonary mass			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Rales			

subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	2 / 24 (8.33%)
occurrences (all)	1	0	2
Rhinorrhoea			
subjects affected / exposed	1 / 79 (1.27%)	2 / 64 (3.13%)	1 / 24 (4.17%)
occurrences (all)	2	2	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	8 / 79 (10.13%)	5 / 64 (7.81%)	2 / 24 (8.33%)
occurrences (all)	10	10	2
Anxiety			
subjects affected / exposed	8 / 79 (10.13%)	3 / 64 (4.69%)	0 / 24 (0.00%)
occurrences (all)	8	3	0
Depression			
subjects affected / exposed	2 / 79 (2.53%)	5 / 64 (7.81%)	0 / 24 (0.00%)
occurrences (all)	2	5	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	11 / 79 (13.92%)	4 / 64 (6.25%)	2 / 24 (8.33%)
occurrences (all)	43	8	2
Platelet count decreased			
subjects affected / exposed	5 / 79 (6.33%)	4 / 64 (6.25%)	2 / 24 (8.33%)
occurrences (all)	38	6	3
Weight decreased			
subjects affected / exposed	6 / 79 (7.59%)	3 / 64 (4.69%)	0 / 24 (0.00%)
occurrences (all)	8	3	0
Blood creatinine increased			
subjects affected / exposed	6 / 79 (7.59%)	3 / 64 (4.69%)	0 / 24 (0.00%)
occurrences (all)	8	7	0
Lipase increased			
subjects affected / exposed	6 / 79 (7.59%)	3 / 64 (4.69%)	0 / 24 (0.00%)
occurrences (all)	10	7	0
Blood alkaline phosphatase increased			
subjects affected / exposed	5 / 79 (6.33%)	3 / 64 (4.69%)	1 / 24 (4.17%)
occurrences (all)	16	3	1
Amylase increased			

subjects affected / exposed	1 / 79 (1.27%)	3 / 64 (4.69%)	0 / 24 (0.00%)
occurrences (all)	2	6	0
Aspartate aminotransferase increased			
subjects affected / exposed	12 / 79 (15.19%)	4 / 64 (6.25%)	1 / 24 (4.17%)
occurrences (all)	37	4	1
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 79 (3.80%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	4	0	0
Haemoglobin decreased			
subjects affected / exposed	2 / 79 (2.53%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	3	0	0
Weight increased			
subjects affected / exposed	2 / 79 (2.53%)	3 / 64 (4.69%)	0 / 24 (0.00%)
occurrences (all)	6	3	0
White blood cell count decreased			
subjects affected / exposed	3 / 79 (3.80%)	4 / 64 (6.25%)	1 / 24 (4.17%)
occurrences (all)	5	15	1
Blood urea increased			
subjects affected / exposed	2 / 79 (2.53%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	4	2	0
Blood uric acid increased			
subjects affected / exposed	4 / 79 (5.06%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences (all)	6	0	2
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 79 (2.53%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Globulins decreased			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Haematocrit decreased			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			

subjects affected / exposed	3 / 79 (3.80%)	1 / 64 (1.56%)	2 / 24 (8.33%)
occurrences (all)	5	1	3
White blood cells urine positive			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 79 (2.53%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Procedural pain			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	4 / 79 (5.06%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	7	1	0
Mitral valve incompetence			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 79 (0.00%)	4 / 64 (6.25%)	0 / 24 (0.00%)
occurrences (all)	0	5	0
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 79 (15.19%)	13 / 64 (20.31%)	6 / 24 (25.00%)
occurrences (all)	18	18	7
Dizziness			
subjects affected / exposed	11 / 79 (13.92%)	7 / 64 (10.94%)	2 / 24 (8.33%)
occurrences (all)	11	7	2
Hypoaesthesia			
subjects affected / exposed	3 / 79 (3.80%)	2 / 64 (3.13%)	1 / 24 (4.17%)
occurrences (all)	3	2	3
Paraesthesia			
subjects affected / exposed	2 / 79 (2.53%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	3	1	0
Dysgeusia			

subjects affected / exposed	2 / 79 (2.53%)	1 / 64 (1.56%)	1 / 24 (4.17%)
occurrences (all)	2	1	1
Neuropathy peripheral			
subjects affected / exposed	3 / 79 (3.80%)	1 / 64 (1.56%)	1 / 24 (4.17%)
occurrences (all)	3	1	1
Sensory disturbance			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	2 / 79 (2.53%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	2	1	0
Syncope			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	2 / 24 (8.33%)
occurrences (all)	1	0	2
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	35 / 79 (44.30%)	18 / 64 (28.13%)	5 / 24 (20.83%)
occurrences (all)	170	104	8
Anaemia			
subjects affected / exposed	33 / 79 (41.77%)	19 / 64 (29.69%)	10 / 24 (41.67%)
occurrences (all)	98	75	16
Neutropenia			
subjects affected / exposed	12 / 79 (15.19%)	16 / 64 (25.00%)	2 / 24 (8.33%)
occurrences (all)	67	39	2
Leukopenia			
subjects affected / exposed	7 / 79 (8.86%)	9 / 64 (14.06%)	2 / 24 (8.33%)
occurrences (all)	19	17	6
Leukocytosis			
subjects affected / exposed	4 / 79 (5.06%)	4 / 64 (6.25%)	2 / 24 (8.33%)
occurrences (all)	6	4	2
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 79 (1.27%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	1	1	0
Eye disorders			

Eye oedema			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Scleral haemorrhage			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Visual acuity reduced			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	67 / 79 (84.81%)	41 / 64 (64.06%)	15 / 24 (62.50%)
occurrences (all)	243	128	29
Nausea			
subjects affected / exposed	36 / 79 (45.57%)	30 / 64 (46.88%)	12 / 24 (50.00%)
occurrences (all)	97	57	19
Vomiting			
subjects affected / exposed	35 / 79 (44.30%)	26 / 64 (40.63%)	11 / 24 (45.83%)
occurrences (all)	75	45	19
Abdominal pain			
subjects affected / exposed	19 / 79 (24.05%)	11 / 64 (17.19%)	3 / 24 (12.50%)
occurrences (all)	26	26	3
Abdominal pain upper			
subjects affected / exposed	9 / 79 (11.39%)	7 / 64 (10.94%)	0 / 24 (0.00%)
occurrences (all)	16	15	0
Constipation			
subjects affected / exposed	14 / 79 (17.72%)	9 / 64 (14.06%)	4 / 24 (16.67%)
occurrences (all)	25	11	5
Dyspepsia			
subjects affected / exposed	9 / 79 (11.39%)	1 / 64 (1.56%)	1 / 24 (4.17%)
occurrences (all)	12	2	1
Abdominal distension			
subjects affected / exposed	1 / 79 (1.27%)	4 / 64 (6.25%)	0 / 24 (0.00%)
occurrences (all)	1	6	0
Flatulence			

subjects affected / exposed	2 / 79 (2.53%)	2 / 64 (3.13%)	0 / 24 (0.00%)
occurrences (all)	2	3	0
Abdominal discomfort			
subjects affected / exposed	4 / 79 (5.06%)	1 / 64 (1.56%)	2 / 24 (8.33%)
occurrences (all)	4	1	2
Toothache			
subjects affected / exposed	3 / 79 (3.80%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	3	0	0
Aphthous stomatitis			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal sounds abnormal			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	1 / 24 (4.17%)
occurrences (all)	0	1	2
Gingival pain			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	4 / 79 (5.06%)	2 / 64 (3.13%)	1 / 24 (4.17%)
occurrences (all)	4	2	1
Mouth ulceration			
subjects affected / exposed	1 / 79 (1.27%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	1	1	0
Stomatitis			
subjects affected / exposed	2 / 79 (2.53%)	2 / 64 (3.13%)	2 / 24 (8.33%)
occurrences (all)	2	2	2
Tongue oedema			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	2 / 79 (2.53%)	5 / 64 (7.81%)	1 / 24 (4.17%)
occurrences (all)	2	8	1

Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	27 / 79 (34.18%)	20 / 64 (31.25%)	4 / 24 (16.67%)
occurrences (all)	53	24	6
Pruritus			
subjects affected / exposed	6 / 79 (7.59%)	4 / 64 (6.25%)	0 / 24 (0.00%)
occurrences (all)	19	4	0
Dry skin			
subjects affected / exposed	3 / 79 (3.80%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	3	1	0
Skin lesion			
subjects affected / exposed	4 / 79 (5.06%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	8	1	0
Alopecia			
subjects affected / exposed	1 / 79 (1.27%)	2 / 64 (3.13%)	0 / 24 (0.00%)
occurrences (all)	1	2	0
Night sweats			
subjects affected / exposed	2 / 79 (2.53%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Angioedema			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	2 / 79 (2.53%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	2	1	0
Ecchymosis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	4 / 79 (5.06%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	6	1	0
Hyperhidrosis			
subjects affected / exposed	2 / 79 (2.53%)	3 / 64 (4.69%)	0 / 24 (0.00%)
occurrences (all)	3	5	0
Nail disorder			

subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	1 / 79 (1.27%)	3 / 64 (4.69%)	3 / 24 (12.50%)
occurrences (all)	2	3	4
Skin burning sensation			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Skin depigmentation			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Swelling face			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 79 (1.27%)	2 / 64 (3.13%)	1 / 24 (4.17%)
occurrences (all)	1	3	1
Pollakiuria			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Renal failure			
subjects affected / exposed	5 / 79 (6.33%)	1 / 64 (1.56%)	1 / 24 (4.17%)
occurrences (all)	5	1	1
Urinary retention			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	12 / 79 (15.19%)	8 / 64 (12.50%)	3 / 24 (12.50%)
occurrences (all)	24	11	4
Back pain			
subjects affected / exposed	8 / 79 (10.13%)	4 / 64 (6.25%)	4 / 24 (16.67%)
occurrences (all)	13	7	4
Pain in extremity			

subjects affected / exposed	9 / 79 (11.39%)	6 / 64 (9.38%)	3 / 24 (12.50%)
occurrences (all)	18	8	4
Myalgia			
subjects affected / exposed	7 / 79 (8.86%)	6 / 64 (9.38%)	2 / 24 (8.33%)
occurrences (all)	7	8	2
Bone pain			
subjects affected / exposed	1 / 79 (1.27%)	7 / 64 (10.94%)	3 / 24 (12.50%)
occurrences (all)	1	8	4
Musculoskeletal pain			
subjects affected / exposed	5 / 79 (6.33%)	3 / 64 (4.69%)	1 / 24 (4.17%)
occurrences (all)	7	6	1
Muscle spasms			
subjects affected / exposed	4 / 79 (5.06%)	1 / 64 (1.56%)	2 / 24 (8.33%)
occurrences (all)	5	1	4
Groin pain			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	1 / 79 (1.27%)	1 / 64 (1.56%)	1 / 24 (4.17%)
occurrences (all)	1	1	1
Musculoskeletal chest pain			
subjects affected / exposed	3 / 79 (3.80%)	1 / 64 (1.56%)	1 / 24 (4.17%)
occurrences (all)	3	1	1
Musculoskeletal stiffness			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	1 / 79 (1.27%)	4 / 64 (6.25%)	0 / 24 (0.00%)
occurrences (all)	2	5	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 79 (8.86%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	9	1	0
Upper respiratory tract infection			
subjects affected / exposed	8 / 79 (10.13%)	2 / 64 (3.13%)	0 / 24 (0.00%)
occurrences (all)	19	3	0

Influenza			
subjects affected / exposed	5 / 79 (6.33%)	0 / 64 (0.00%)	1 / 24 (4.17%)
occurrences (all)	9	0	1
Urinary tract infection			
subjects affected / exposed	1 / 79 (1.27%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	5	1	0
Bronchitis			
subjects affected / exposed	6 / 79 (7.59%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	6	0	0
Sinusitis			
subjects affected / exposed	1 / 79 (1.27%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal infection			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Gingivitis			
subjects affected / exposed	0 / 79 (0.00%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	4 / 79 (5.06%)	2 / 64 (3.13%)	0 / 24 (0.00%)
occurrences (all)	4	2	0
Oral herpes			
subjects affected / exposed	6 / 79 (7.59%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	6	1	0
Pharyngitis			
subjects affected / exposed	1 / 79 (1.27%)	1 / 64 (1.56%)	0 / 24 (0.00%)
occurrences (all)	1	1	0
Pneumonia			
subjects affected / exposed	2 / 79 (2.53%)	4 / 64 (6.25%)	1 / 24 (4.17%)
occurrences (all)	2	4	1
Respiratory tract infection viral			
subjects affected / exposed	2 / 79 (2.53%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0

Wound infection			
subjects affected / exposed	0 / 79 (0.00%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	7 / 79 (8.86%)	12 / 64 (18.75%)	1 / 24 (4.17%)
occurrences (all)	15	12	2
Hypokalaemia			
subjects affected / exposed	2 / 79 (2.53%)	6 / 64 (9.38%)	2 / 24 (8.33%)
occurrences (all)	8	10	4
Hypophosphataemia			
subjects affected / exposed	5 / 79 (6.33%)	3 / 64 (4.69%)	2 / 24 (8.33%)
occurrences (all)	12	6	2
Hyperuricaemia			
subjects affected / exposed	3 / 79 (3.80%)	2 / 64 (3.13%)	0 / 24 (0.00%)
occurrences (all)	3	8	0
Hypocalcaemia			
subjects affected / exposed	2 / 79 (2.53%)	5 / 64 (7.81%)	1 / 24 (4.17%)
occurrences (all)	2	8	1
Hyperglycaemia			
subjects affected / exposed	4 / 79 (5.06%)	1 / 64 (1.56%)	2 / 24 (8.33%)
occurrences (all)	6	2	2
Hyperkalaemia			
subjects affected / exposed	4 / 79 (5.06%)	3 / 64 (4.69%)	0 / 24 (0.00%)
occurrences (all)	11	4	0
Hypernatraemia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Hypoglycaemia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 64 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Hypomagnesaemia			
subjects affected / exposed	2 / 79 (2.53%)	4 / 64 (6.25%)	0 / 24 (0.00%)
occurrences (all)	2	4	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 October 2006	This amendment updated the protocol with new safety and efficacy information. This amendment also increased the size of the MTD cohort (i.e., those enrolled at Part 2) to approximately 330 participants.
10 June 2008	Removed physical examination at Week 12 and q12 week visits. Removed pharmacodynamic and pharmacogenomic testing in Part 2. Added requirement that participants in Taiwan will be monitored with ECGs every 12 weeks during treatment in order to accommodate the request of local regulatory authorities. Removed the pharmacokinetic sample collected at Week 2. Updated the background information about imatinib. Added background information for dasatinib and nilotinib. Added rationale for inclusion of participants who have failed dasatinib or nilotinib. Updated the data for Phase 1 study 3160A1-100-US in solid tumor participants. Provided an update on interim analyses of efficacy that were performed on all cohorts meeting pre-specified targets of evaluable participants enrolled. Provided a rationale to exclude participants with known T315I mutation. Modified previous objective to include newly added CP nilotinib-resistant cohort. Added a secondary endpoint for the new AP and BP cohorts. Added imatinib-resistant/intolerant and nilotinib-resistant participants to the CP exploratory cohorts. Added explanation of treatment of initial participants in China in order to accommodate the request of local regulatory authorities. Added guidance regarding systemic steroid use and potassium and magnesium supplementation. Removed Vitamin K and PIVKA-II testing for participants with grade 2 increased INR or >1 unit (if taking OAT), as this testing is not readily available at most institutions. Other minor changes such as further clarifications, protocol section renumbering, and corrections of spelling and grammatical errors were added throughout the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Analyses of progression free survival and overall survival was based on all-treated population, instead of evaluable population which was the primary efficacy population as per planned analyses.

Notes: