Clinical trial results:
An Open-Label Bosutinib Treatment Extension Study for Subjects With Chronic Myeloid Leukemia (CML) Who Have Previously Participated in Bosutinib Studies B1871006 or B1871008

Summary

EudraCT number	2013-000691-15
Trial protocol	IT HU LT LV NL FI ES GB FR BE PL
Global end of trial date	05 June 2020

Results information

Result version number	v1 (current)
This version publication date	20 June 2021
First version publication date	20 June 2021

Trial information

Trial identification

Sponsor protocol code	B1871040

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01903733
WHO universal trial number (UTN)	-

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 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, 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	05 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 June 2020
Global end of trial reached?	Yes
Global end of trial date	05 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To allow long-term bosutinib treatment in subjects with chronic phase (CP) or advanced (ADV) phase Philadelphia chromosome-positive (Ph+) CML who received bosutinib in a previous Pfizer sponsored CML study (ie, studies B1871006 and B1871008) and who have the potential, as judged by the investigator, to derive clinical benefit from continued treatment with bosutinib.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 August 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	10 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 24
Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Brazil: 35
Country: Number of subjects enrolled	Canada: 21
Country: Number of subjects enrolled	Chile: 2
Country: Number of subjects enrolled	China: 51
Country: Number of subjects enrolled	Colombia: 8
Country: Number of subjects enrolled	Germany: 49
Country: Number of subjects enrolled	Spain: 19
Country: Number of subjects enrolled	Finland: 7
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	United Kingdom: 12
Country: Number of subjects enrolled	Hong Kong: 10
Country: Number of subjects enrolled	Hungary: 14
Country: Number of subjects enrolled	India: 47

Country: Number of subjects enrolled	Italy: 61
Country: Number of subjects enrolled	Japan: 15
Country: Number of subjects enrolled	Korea, Republic of: 45
Country: Number of subjects enrolled	Lithuania: 7
Country: Number of subjects enrolled	Latvia: 2
Country: Number of subjects enrolled	Mexico: 5
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	Poland: 13
Country: Number of subjects enrolled	Russian Federation: 94
Country: Number of subjects enrolled	Singapore: 15
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	Thailand: 4
Country: Number of subjects enrolled	Turkey: 6
Country: Number of subjects enrolled	Taiwan: 3
Country: Number of subjects enrolled	Ukraine: 25
Country: Number of subjects enrolled	United States: 165
Country: Number of subjects enrolled	South Africa: 9
Worldwide total number of subjects	820
EEA total number of subjects	209

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)	662
From 65 to 84 years	155
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Study included subjects randomised to bosutinib arm in B1871008 or dosed with bosutinib in B1871006. Subjects enrolled were who in any parent study at time of protocol approval 1) receiving bosutinib, benefiting per investigator, 2) discontinued bosutinib, being followed-up, 3) completed parent study. 281 subjects were enrolled, 21 were from China.

Pre-assignment

Screening details:

Data from the 2 parent studies were combined with data from this study for all analyses. The B1871040 data from 21 subjects enrolled in China were not used in results as approval was not obtained to use the data per HGRAC regulations. Reporting arms were based on parent study, disease phase and line of therapy (CP1L, CP2L, CP3L/CP4L, ADV).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Bosutinib, CP1L

Arm description:

Subjects from B1871008 with Ph+ chronic phase 1st line (CP1L) CML who either continued to receive the same bosutinib dose as at the time of completion of B1871008 or continued to be followed for survival. Dose for bosutinib was 500 milligram (mg) orally once daily (adjusted dose varied from 200 mg to 600 mg once daily). Treatment continued until the end of the study, disease progression, unacceptable toxicity, death, withdrawal of consent or study discontinuation whichever occurred first. Follow-up continued till end of the study or death due to any cause whichever occurred first. Subjects remained in this study, either for treatment or for follow-up, until the last subject enrolled in 1 of the parent studies reached 10 years of follow-up, as calculated from the date of his/her first dose of bosutinib administered in parent 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:

Subjects received bosutinib at a dose of 500 mg, orally once daily (adjusted dose varied from 200 mg to 600 mg once daily).

Arm title	Bosutinib, CP2L

Arm description:

Subjects from B1871006 with Ph+ chronic phase 2nd line (CP2L) CML who were resistant or intolerant to imatinib either continued to receive the same bosutinib dose as at the time of completion of B1871006 or continued to be followed for survival. Dose for bosutinib was 500 mg orally once daily (adjusted dose varied from 200 mg to 600 mg once daily). Treatment continued until the end of the study, disease progression, unacceptable toxicity, death, withdrawal of consent or study discontinuation whichever occurred first. Follow-up continued till end of the study or death due to any cause whichever occurred first. Subjects remained in this study, either for treatment or for follow-up, until the last subject enrolled in 1 of the parent studies reached 10 years of follow-up, as calculated from the date of his/her first dose of bosutinib administered in parent 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:

Subjects received bosutinib at a dose of 500 mg, orally once daily (adjusted dose varied from 200 mg to 600 mg once daily).

Arm title	Bosutinib, CP3L/CP4L

Arm description:

Subjects from B1871006 with Ph+ chronic phase 3rd line (CP3L)/4th line (CP4L) CML who were resistant or intolerant to imatinib and resistant or intolerant to dasatinib and/or nilotinib either continued to receive the same bosutinib dose as at the time of completion of B1871006 or continued to be followed for survival. Dose for bosutinib was 500 mg orally once daily (adjusted dose varied from 200 mg to 600 mg once daily). Treatment continued until the end of the study, disease progression, unacceptable toxicity, death, withdrawal of consent or study discontinuation whichever occurred first. Follow-up continued till end of the study or death due to any cause whichever occurred first. Subjects remained in this study, either for treatment or for follow-up, until the last subject enrolled in 1 of the parent studies reached 10 years of follow-up, as calculated from the date of his/her first dose of bosutinib administered in parent 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:

Subjects received bosutinib at a dose of 500 mg, orally once daily (adjusted dose varied from 200 mg to 600 mg once daily).

Arm title	Bosutinib, ADV

Arm description:

ADV subjects from B1871006 with Ph+ accelerated phase(AP),blast phase(BP) CML, Ph+ acute lymphoblastic leukemia(ALL) and resistant or intolerant(R/I) to imatinib only or R/I to imatinib and at least 1 additional tyrosine kinase inhibitor(TKI) including dasatinib and/or nilotinib who either continued to receive same bosutinib dose as at time of completion of B1871008 or continued to be followed for survival. Dose for bosutinib was 500 mg orally once daily(od) (adjusted dose varied from 200 mg to 600 mg od). Treatment continued until end of study, disease progression,unacceptable toxicity,death,withdrawal of consent or study discontinuation whichever occurred first. Follow-up continued till end of study or death due to any cause whichever occurred first. Subjects remained in study, either for treatment or for follow-up,until last subject enrolled in 1 of parent studies reached 10 years of follow-up, as calculated from date of his/her first dose of bosutinib administered in parent

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:

Subjects received bosutinib at a dose of 500 mg, orally once daily (adjusted dose varied from 200 mg to 600 mg once daily).

Number of subjects in period 1	Bosutinib, CP1L	Bosutinib, CP2L	Bosutinib, CP3L/CP4L
Started	250	284	119
Full analysis set	250	284	119
Safety analysis set	248	284	119
Enrolled in B1871040	124 [1]	90 [2]	28 [3]
Treated in B1871040	98 [4]	69 [5]	13 [6]
Completed	144	158	58
Not completed	106	126	61
Adverse event, serious fatal	23	54	30
Unspecified	10	15	12
Subject refused further follow-up	35	38	13
Lost to follow-up	18	19	6
Missing	2	-	-
Investigator request	18	-	-

Number of subjects in period 1	Bosutinib, ADV
Started	167
Full analysis set	167
Safety analysis set	167
Enrolled in B1871040	18 [7]
Treated in B1871040	8 [8]
Completed	48
Not completed	119
Adverse event, serious fatal	98
Unspecified	3
Subject refused further follow-up	9
Lost to follow-up	9
Missing	-
Investigator request	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This milestone depicts number of subjects enrolled specifically in this study excluding subjects enrolled in China.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This milestone depicts number of subjects enrolled specifically in this study excluding subjects enrolled in China.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This milestone depicts number of subjects enrolled specifically in this study excluding subjects enrolled in China.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This milestone depicts number of subjects enrolled specifically in this study excluding subjects enrolled in China.
[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This milestone depicts number of subjects enrolled specifically in this study excluding subjects enrolled in China.
[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This milestone depicts number of subjects enrolled specifically in this study excluding subjects enrolled in China.
[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This milestone depicts number of subjects enrolled specifically in this study excluding subjects enrolled in China.
[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This milestone depicts number of subjects enrolled specifically in this study excluding subjects enrolled in China.

Baseline characteristics

Reporting groups

Reporting group title	Bosutinib, CP1L

Reporting group description:

Subjects from B1871008 with Ph+ chronic phase 1st line (CP1L) CML who either continued to receive the same bosutinib dose as at the time of completion of B1871008 or continued to be followed for survival. Dose for bosutinib was 500 milligram (mg) orally once daily (adjusted dose varied from 200 mg to 600 mg once daily). Treatment continued until the end of the study, disease progression, unacceptable toxicity, death, withdrawal of consent or study discontinuation whichever occurred first. Follow-up continued till end of the study or death due to any cause whichever occurred first. Subjects remained in this study, either for treatment or for follow-up, until the last subject enrolled in 1 of the parent studies reached 10 years of follow-up, as calculated from the date of his/her first dose of bosutinib administered in parent study.

Reporting group title	Bosutinib, CP2L

Reporting group description:

Subjects from B1871006 with Ph+ chronic phase 2nd line (CP2L) CML who were resistant or intolerant to imatinib either continued to receive the same bosutinib dose as at the time of completion of B1871006 or continued to be followed for survival. Dose for bosutinib was 500 mg orally once daily (adjusted dose varied from 200 mg to 600 mg once daily). Treatment continued until the end of the study, disease progression, unacceptable toxicity, death, withdrawal of consent or study discontinuation whichever occurred first. Follow-up continued till end of the study or death due to any cause whichever occurred first. Subjects remained in this study, either for treatment or for follow-up, until the last subject enrolled in 1 of the parent studies reached 10 years of follow-up, as calculated from the date of his/her first dose of bosutinib administered in parent study.

Reporting group title	Bosutinib, CP3L/CP4L

Reporting group description:

Subjects from B1871006 with Ph+ chronic phase 3rd line (CP3L)/4th line (CP4L) CML who were resistant or intolerant to imatinib and resistant or intolerant to dasatinib and/or nilotinib either continued to receive the same bosutinib dose as at the time of completion of B1871006 or continued to be followed for survival. Dose for bosutinib was 500 mg orally once daily (adjusted dose varied from 200 mg to 600 mg once daily). Treatment continued until the end of the study, disease progression, unacceptable toxicity, death, withdrawal of consent or study discontinuation whichever occurred first. Follow-up continued till end of the study or death due to any cause whichever occurred first. Subjects remained in this study, either for treatment or for follow-up, until the last subject enrolled in 1 of the parent studies reached 10 years of follow-up, as calculated from the date of his/her first dose of bosutinib administered in parent study.

Reporting group title	Bosutinib, ADV

Reporting group description:

ADV subjects from B1871006 with Ph+ accelerated phase(AP),blast phase(BP) CML, Ph+ acute lymphoblastic leukemia(ALL) and resistant or intolerant(R/I) to imatinib only or R/I to imatinib and at least 1 additional tyrosine kinase inhibitor(TKI) including dasatinib and/or nilotinib who either continued to receive same bosutinib dose as at time of completion of B1871008 or continued to be followed for survival. Dose for bosutinib was 500 mg orally once daily(od) (adjusted dose varied from 200 mg to 600 mg od). Treatment continued until end of study, disease progression,unacceptable toxicity,death,withdrawal of consent or study discontinuation whichever occurred first. Follow-up continued till end of study or death due to any cause whichever occurred first. Subjects remained in study, either for treatment or for follow-up,until last subject enrolled in 1 of parent studies reached 10 years of follow-up, as calculated from date of his/her first dose of bosutinib administered in parent

Reporting group values	Bosutinib, CP1L	Bosutinib, CP2L	Bosutinib, CP3L/CP4L
Number of subjects	250	284	119
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0

Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	220	217	91
From 65-84 years	29	65	28
85 years and over	1	2	0
Age Continuous			
Units: Years			
arithmetic mean	47.9	51.9	55.1
standard deviation	± 14.4	± 15.1	± 13.0
Sex: Female, Male			
Units: Subjects			
Female	101	135	66
Male	149	149	53
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	83	61	15
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	16	6
White	160	186	87
More than one race	0	0	0
Unknown or Not Reported	5	20	11

Reporting group values	Bosutinib, ADV	Total	
Number of subjects	167	820	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	134	662	
From 65-84 years	33	155	
85 years and over	0	3	
Age Continuous			
Units: Years			
arithmetic mean	50.1		
standard deviation	± 15.4	-	
Sex: Female, Male			
Units: Subjects			
Female	69	371	
Male	98	449	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	1	
Asian	37	196	

Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	19	43	
White	102	535	
More than one race	0	0	
Unknown or Not Reported	9	45	

End points reporting groups

Reporting group title	Bosutinib, CP1L

Reporting group description:

Subjects from B1871008 with Ph+ chronic phase 1st line (CP1L) CML who either continued to receive the same bosutinib dose as at the time of completion of B1871008 or continued to be followed for survival. Dose for bosutinib was 500 milligram (mg) orally once daily (adjusted dose varied from 200 mg to 600 mg once daily). Treatment continued until the end of the study, disease progression, unacceptable toxicity, death, withdrawal of consent or study discontinuation whichever occurred first. Follow-up continued till end of the study or death due to any cause whichever occurred first. Subjects remained in this study, either for treatment or for follow-up, until the last subject enrolled in 1 of the parent studies reached 10 years of follow-up, as calculated from the date of his/her first dose of bosutinib administered in parent study.

Reporting group title	Bosutinib, CP2L

Reporting group description:

Subjects from B1871006 with Ph+ chronic phase 2nd line (CP2L) CML who were resistant or intolerant to imatinib either continued to receive the same bosutinib dose as at the time of completion of B1871006 or continued to be followed for survival. Dose for bosutinib was 500 mg orally once daily (adjusted dose varied from 200 mg to 600 mg once daily). Treatment continued until the end of the study, disease progression, unacceptable toxicity, death, withdrawal of consent or study discontinuation whichever occurred first. Follow-up continued till end of the study or death due to any cause whichever occurred first. Subjects remained in this study, either for treatment or for follow-up, until the last subject enrolled in 1 of the parent studies reached 10 years of follow-up, as calculated from the date of his/her first dose of bosutinib administered in parent study.

Reporting group title	Bosutinib, CP3L/CP4L

Reporting group description:

Subjects from B1871006 with Ph+ chronic phase 3rd line (CP3L)/4th line (CP4L) CML who were resistant or intolerant to imatinib and resistant or intolerant to dasatinib and/or nilotinib either continued to receive the same bosutinib dose as at the time of completion of B1871006 or continued to be followed for survival. Dose for bosutinib was 500 mg orally once daily (adjusted dose varied from 200 mg to 600 mg once daily). Treatment continued until the end of the study, disease progression, unacceptable toxicity, death, withdrawal of consent or study discontinuation whichever occurred first. Follow-up continued till end of the study or death due to any cause whichever occurred first. Subjects remained in this study, either for treatment or for follow-up, until the last subject enrolled in 1 of the parent studies reached 10 years of follow-up, as calculated from the date of his/her first dose of bosutinib administered in parent study.

Reporting group title	Bosutinib, ADV

Reporting group description:

ADV subjects from B1871006 with Ph+ accelerated phase(AP),blast phase(BP) CML, Ph+ acute lymphoblastic leukemia(ALL) and resistant or intolerant(R/I) to imatinib only or R/I to imatinib and at least 1 additional tyrosine kinase inhibitor(TKI) including dasatinib and/or nilotinib who either continued to receive same bosutinib dose as at time of completion of B1871008 or continued to be followed for survival. Dose for bosutinib was 500 mg orally once daily(od) (adjusted dose varied from 200 mg to 600 mg od). Treatment continued until end of study, disease progression,unacceptable toxicity,death,withdrawal of consent or study discontinuation whichever occurred first. Follow-up continued till end of study or death due to any cause whichever occurred first. Subjects remained in study, either for treatment or for follow-up,until last subject enrolled in 1 of parent studies reached 10 years of follow-up, as calculated from date of his/her first dose of bosutinib administered in parent

Subject analysis set title	Bosutinib 200 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received uninterrupted once daily oral 200 mg dose of bosutinib for at least 2 weeks in study B1871040.

Subject analysis set title	Bosutinib 300 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received uninterrupted once daily oral 300 mg dose of bosutinib for at least 2 weeks in study B1871040.

Subject analysis set title	Bosutinib 400 mg

Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received uninterrupted once daily oral 400 mg dose of bosutinib for at least 2 weeks in study B1871040.

Subject analysis set title	Bosutinib 500 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received uninterrupted once daily oral 500 mg dose of bosutinib for at least 2 weeks in study B1871040.

Subject analysis set title	Bosutinib 600 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received uninterrupted once daily oral 600 mg dose of bosutinib for at least 2 weeks in study B1871040.

Subject analysis set title	Bosutinib, Total
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects from B1871008 CP1L cohort and B1871006 CP2L, CP3L/CP4L and ADV cohorts.

Primary: Number of Subjects With Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs) Based on National Cancer Institute Common Terminology Criteria for AEs (NCI CTCAE) (Version 3.0)

End point title	Number of Subjects With Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs) Based on National Cancer Institute Common Terminology Criteria for AEs (NCI CTCAE) (Version 3.0)[1]

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. SAE was any untoward medical occurrence at any dose that: resulted in death, was life threatening (immediate risk of death), required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions), resulted in congenital anomaly/birth defect. Treatment-emergent adverse events were defined as any event increasing in severity from baseline or any new event started during bosutinib therapy or within 30 days of the last dose of study drug. Safety analysis set included all dosed subjects for both B1871006 and B1871008.

End point type	Primary

End point timeframe:

From first dose of drug up to 30 days after last dose (up to approximately 14 years)

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 endpoint reports data for B1871006 subjects.

End point values	Bosutinib, CP1L	Bosutinib, CP2L	Bosutinib, CP3L/CP4L	Bosutinib, ADV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	248	284	119	167
Units: subjects				
Treatment-Emergent AEs	241	283	119	165
Treatment-emergent SAEs	102	124	44	98

End point values	Bosutinib, Total			

Subject group type	Subject analysis set			
Number of subjects analysed	818			
Units: subjects				
Treatment-Emergent AEs	808			
Treatment-emergent SAEs	368			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Grade 3 or 4 Treatment-Emergent Adverse Events (AEs) Based on National Cancer Institute Common Terminology Criteria for AEs (NCI CTCAE) (Version 3.0)

End point title	Number of Subjects With Grade 3 or 4 Treatment-Emergent Adverse Events (AEs) Based on National Cancer Institute Common Terminology Criteria for AEs (NCI CTCAE) (Version 3.0)[2]

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. AEs were assessed according to severity grading based on NCI CTCAE version 3.0. Grade 1 =mild; Grade 2 =moderate; Grade 3 =severe or medically significant but not immediately life-threatening, hospitalisation or prolongation of hospitalisation indicated; Grade 4 =life-threatening or disabling, urgent intervention indicated; Grade 5 =death. Treatment-emergent adverse events were defined as any event increasing in severity from baseline or any new event started during bosutinib therapy or within 30 days of the last dose of study drug. Safety analysis set included all dosed subjects for both B1871006 and B1871008.

End point type	Primary

End point timeframe:

From first dose of drug up to 30 days after last dose (up to approximately 14 years)

Notes:

[2] - 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 endpoint reports data for B1871006 subjects.

End point values	Bosutinib, CP1L	Bosutinib, CP2L	Bosutinib, CP3L/CP4L	Bosutinib, ADV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	248	284	119	167
Units: subjects	191	223	84	144

End point values	Bosutinib, Total			
Subject group type	Subject analysis set			
Number of subjects analysed	818			
Units: subjects	642			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Treatment-Emergent Treatment Related Adverse Events (AEs) Based on National Cancer Institute Common Terminology Criteria for AEs (NCI CTCAE) (Version 3.0)

End point title	Number of Subjects With Treatment-Emergent Treatment Related Adverse Events (AEs) Based on National Cancer Institute Common Terminology Criteria for AEs (NCI CTCAE) (Version 3.0)[3]

End point description:

An AE was any untoward medical occurrence in a subject who received study drug. Treatment-emergent adverse events were defined as any event increasing in severity from baseline or any new event started during bosutinib therapy or within 30 days of the last dose of study drug. Related TEAEs were those AEs who were related to the study treatment as judged by the investigator. Safety analysis set included all dosed subjects for both B1871006 and B1871008.

End point type	Primary

End point timeframe:

From first dose of drug up to 30 days after last dose (up to approximately 14 years)

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 endpoint reports data for B1871006 subjects.

End point values	Bosutinib, CP1L	Bosutinib, CP2L	Bosutinib, CP3L/CP4L	Bosutinib, ADV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	248	284	119	167
Units: subjects	235	282	119	161

End point values	Bosutinib, Total			
Subject group type	Subject analysis set			
Number of subjects analysed	818			
Units: subjects	797			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Laboratory Test Abnormalities Based on National Cancer Institute Common Terminology Criteria for AEs (NCI CTCAE) (Version 4.03)

End point title	Number of Subjects With Laboratory Test Abnormalities Based on National Cancer Institute Common Terminology Criteria for AEs (NCI CTCAE) (Version 4.03)[4]

End point description:

Laboratory parameters were evaluated as per NCI CTCAE version 4.03 and included Chemistry: high alkaline phosphatase; high alanine aminotransferase; high aspartate aminotransferase; high blood bilirubin; high creatinine. Hematology: absolute neutrophils count decreased; anemia; platelet count decreased; WBC decreased. Safety analysis set included all dosed subjects for both B1871006 and B1871008.

End point type	Primary

End point timeframe:

From first dose of drug up to 30 days after last dose (up to approximately 14 years)

Notes:

[4] - 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 endpoint reports data for B1871006 subjects.

End point values	Bosutinib, CP1L	Bosutinib, CP2L	Bosutinib, CP3L/CP4L	Bosutinib, ADV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	248	284	119	167
Units: subjects				
Grade 1	45	59	28	18
Grade 2	86	80	39	24
Grade 3	84	102	27	41
Grade 4	33	42	23	82

End point values	Bosutinib, Total			
Subject group type	Subject analysis set			
Number of subjects analysed	818			
Units: subjects				
Grade 1	150			
Grade 2	229			
Grade 3	254			
Grade 4	180			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Adverse Events as Reason for Treatment Discontinuation

End point title	Number of Subjects With Adverse Events as Reason for Treatment Discontinuation[5]

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. Safety analysis set included all dosed subjects for both B1871006 and B1871008.

End point type	Primary

End point timeframe:

From first dose of drug up to 30 days after last dose (up to approximately 14 years)

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 endpoint reports data for B1871006 subjects.

End point values	Bosutinib, CP1L	Bosutinib, CP2L	Bosutinib, CP3L/CP4L	Bosutinib, ADV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	248	284	119	167
Units: subjects	84	79	37	32

End point values	Bosutinib, Total			
Subject group type	Subject analysis set			
Number of subjects analysed	818			
Units: subjects	232			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Diarrhea After Switch From Bosutinib Clinical Formulation to Bosutinib Commercial Formulation

End point title	Number of Subjects With Diarrhea After Switch From Bosutinib Clinical Formulation to Bosutinib Commercial Formulation[6]

End point description:

The incidence of diarrhea was collected and analysed before and after the switch from the clinical formulation of bosutinib to the commercial formulation of bosutinib. Safety analysis set included all dosed subjects for both B1871006 and B1871008. Here, 'Overall number of subjects analysed (N)'= subjects evaluable for this endpoint who received commercial formulation.

End point type	Primary

End point timeframe:

Last 6 months on clinical formulation and first 6 months on commercial formulation

Notes:

[6] - 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 endpoint reports data for B1871006 subjects.

End point values	Bosutinib, CP1L	Bosutinib, CP2L	Bosutinib, CP3L/CP4L	Bosutinib, ADV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	119	82	13	8
Units: subjects				
Clinical formulation (last 6 months)	25	22	3	5
Commercial formulation (first 6 months)	34	27	4	5

End point values	Bosutinib, Total			
Subject group type	Subject analysis set			
Number of subjects analysed	222			
Units: subjects				
Clinical formulation (last 6 months)	55			
Commercial formulation (first 6 months)	70			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Breakpoint Cluster Region Abelson Protooncogene (BCR-ABL) Mutations Present at Time of Bosutinib Treatment Discontinuation

End point title	Number of Subjects With Breakpoint Cluster Region Abelson Protooncogene (BCR-ABL) Mutations Present at Time of Bosutinib Treatment Discontinuation[7]

End point description:

BCR-ABL is a gene resulting from the 9:22 chromosomal translocation (Philadelphia chromosome). In this endpoint, the number of subjects who had emergent mutation or new BCR-ABL mutations (subjects who had a post-baseline mutation which was not present at baseline) were reported. The full analysis set included all subjects randomised to the bosutinib arm from B1871008 and all dosed subjects from B1871006.

End point type	Primary

End point timeframe:

Post-baseline on Day 1 (maximum up to 14 years)

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 endpoint reports data for B1871006 subjects.

End point values	Bosutinib, CP1L	Bosutinib, CP2L	Bosutinib, CP3L/CP4L	Bosutinib, ADV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	250	284	119	167
Units: subjects				
Subjects with Emergent mutations	7	28	13	14

Statistical analyses

No statistical analyses for this end point

Primary: Overall Survival (OS) Rate at Year 10

End point title	Overall Survival (OS) Rate at Year 10[8]

End point description:

OS was defined as the time from randomisation (B1871008) and time from first dose (B1871006) to the occurrence of death due to any cause or censoring. Kaplan-Meier analysis was used for determination of OS. Percentage of subjects who were alive were estimated in this endpoint. The full analysis set included all subjects randomised to the bosutinib arm from B1871008 and all dosed subjects from B1871006.

End point type	Primary

End point timeframe:

Year 10

Notes:

[8] - 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 endpoint reports data for B1871006 subjects.

End point values	Bosutinib, CP1L	Bosutinib, CP2L	Bosutinib, CP3L/CP4L	Bosutinib, ADV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	250	284	119	167
Units: percentage of subjects				
number (confidence interval 95%)	88.2 (83.3 to 93.2)	71.5 (64.4 to 78.7)	60.4 (47.2 to 73.7)	34.2 (25.0 to 43.4)

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Steady-State Trough Concentrations (Ctrough) of Bosutinib

End point title	Plasma Steady-State Trough Concentrations (Ctrough) of Bosutinib[9]

End point description:

Ctrough refers to plasma concentration of bosutinib observed just before treatment administration. The pharmacokinetic (PK) analysis set included subjects who received at least 1 dose of bosutinib and had 1 reported bosutinib concentration.

End point type	Primary

End point timeframe:

One pre-dose sample was collected at the first scheduled visit (after approval and implementation of protocol amendment 1) following at least 2 weeks of uninterrupted dosing at the same dose level

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 endpoint reports data for B1871006 subjects.

End point values	Bosutinib 200 mg	Bosutinib 300 mg	Bosutinib 400 mg	Bosutinib 500 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	28	23	69
Units: nanogram per millilitre				
geometric mean (geometric coefficient of variation)	62.2 (± 31.3)	62.0 (± 65.9)	82.2 (± 53.2)	93.3 (± 45.2)

End point values	Bosutinib 600 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: nanogram per millilitre				
geometric mean (geometric coefficient of variation)	99.4 (± 78.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Kaplan-Meier Estimate of Probability of Maintaining Major Cytogenetic Response (MCyR) at Year 10: B1871006 Subjects

End point title	Kaplan-Meier Estimate of Probability of Maintaining Major Cytogenetic Response (MCyR) at Year 10: B1871006 Subjects[10][11]

End point description:

Cytogenetic response(CyR) is based on prevalence of Ph+ cells.MCyR duration:time from first response to confirmed loss, progression of disease or on-treatment death due to any cause or censoring analysed for responders only.Confirmed loss:2 consecutive non-responses >=28 days apart. MCyR was grouped as complete CyR (CCyR) or partial CyR (PCyR).Response was achieved when there was 0% (CCyR) or 1-35% (PCyR) Ph+ cells analysed from conventional cytogenetics based on the analysis of 20 to 100 metaphases or <1% (CCyR) or 1-35% (PCyR) Ph+ cells analysed from FISH based on analysis of >=200 nuclei. CCyR may be imputed on specific date if MMR or better is achieved & denoted on CRF on that date for B1871040 study visits.Kaplan-Meier analysis was used.Evaluable analysis set for cytogenetic population: B1871006 dosed subjects with valid baseline efficacy assessment from B1871006 with >=20 metaphases or >=1 Ph+ metaphase from baseline BM cytogenetic assessment & who achieved MCyR(responders).

End point type	Primary

End point timeframe:

Year 10

Notes:

[10] - 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 endpoint reports data for B1871006 subjects.

[11] - 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: The endpoint reports data for B1871006 subjects.

End point values	Bosutinib, CP2L	Bosutinib, CP3L/CP4L	Bosutinib, ADV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	157	47	54	
Units: percentage of subjects				
number (confidence interval 95%)	65.3 (56.6 to 74.0)	55.3 (36.3 to 74.4)	30.6 (16.4 to 44.7)	

Statistical analyses

No statistical analyses for this end point

Primary: Kaplan-Meier Estimate of Probability of Maintaining Complete Cytogenetic Response (CCyR) at Year 10: B1871006 Subjects

End point title	Kaplan-Meier Estimate of Probability of Maintaining Complete

	Cytogenetic Response (CCyR) at Year 10: B1871006

End point description:

Duration for CCyR was defined as time from first response to confirmed loss, progression of disease, or on-treatment death due to any cause, or censoring analysed for responders only. Confirmed loss was defined as 2 consecutive assessments with >0 Ph+ metaphases or >=1% positive cells from FISH at least 28 days apart or progression or death. CCyR was achieved when there was 0% Ph+ cells analysed from conventional cytogenetics with 20 to 100 metaphases or <1% Ph+ cells analysed from FISH with at least 200 nuclei. CCyR may be imputed on a specific date if MMR or better was achieved and denoted on the CRF on that date for B1871040 study visits. Kaplan-Meier analysis was used. Evaluable analysis set for cytogenetic population were those dosed subjects from B1871006 with a valid baseline efficacy assessment from B1871006 with at least 20 metaphases or at least 1 Ph+ metaphase from the baseline bone marrow cytogenetic assessment and who achieved CCyR (responders).

End point type	Primary

End point timeframe:

Year 10

Notes:

[12] - 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 endpoint reports data for B1871006 subjects.

[13] - 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: The endpoint reports data for B1871006 subjects.

End point values	Bosutinib, CP2L	Bosutinib, CP3L/CP4L	Bosutinib, ADV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	130	36	42	
Units: percentage of subjects				
number (confidence interval 95%)	63.4 (54.0 to 72.8)	40.8 (22.0 to 59.6)	29.6 (14.6 to 44.7)	

Statistical analyses

No statistical analyses for this end point

Primary: Kaplan-Meier Estimate of Probability of Maintaining Complete Hematologic Response (CHR) at Year 10: B1871006 Subjects

End point title	Kaplan-Meier Estimate of Probability of Maintaining Complete Hematologic Response (CHR) at Year 10: B1871006 Subjects[14][15]

End point description:

Duration for CHR:time from first response to confirmed loss, progression of disease or on-treatment death due to any cause or censoring analysed for responders only. Confirmed loss:2 consecutive non-responses >=14 days apart. CHR considered when subjects met all criteria:WBC <=institutional ULN, no blasts or promyelocytes, <20% basophils, no extramedullary involvement (including hepatomegaly or splenomegaly), myelocytes, metamyelocytes <5% in blood, platelets <450*10^9/L. Following were applicable only to advanced phase: <=5% bone marrow blasts, absolute neutrophil count >=1.0*10^9/L, platelets >=100*10^9/L. Kaplan-Meier analysis used. Evaluable analysis set for hematologic population:B1871006 dosed subjects with valid baseline efficacy assessment from B1871006 & valid baseline hematologic assessment & who achieved CHR (responders). 99999=percentage & 95% CI not estimable since BM blasts were not always assessed in later years for

End point type	Primary

End point timeframe:

Year 10

Notes:

[14] - 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 endpoint reports data for B1871006 subjects.

[15] - 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: The endpoint reports data for B1871006 subjects.

End point values	Bosutinib, CP2L	Bosutinib, CP3L/CP4L	Bosutinib, ADV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	245	86	36	
Units: percentage of subjects				
number (confidence interval 95%)	44.1 (35.2 to 52.9)	45.1 (29.3 to 60.9)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Primary: Cumulative Incidence of Progression/Death Events at Year 10: B1871006 Subjects

End point title	Cumulative Incidence of Progression/Death Events at Year 10: B1871006 Subjects[16][17]

End point description:

PFS was defined as interval from date of first dose of bosutinib in parent study until earlier date of progression or death from any cause. Subjects without events censored at last evaluation date. PD evolution from: CP (or return to CP for ADV subjects) to AP or BP (on 2 consecutive assessments >=1 week apart), AP to BP (on 2 consecutive assessments >=1 week apart) and 1 of following conditions: for 2nd or later line, loss of MCyR (>=30% increase); for all lines of treatment: loss of CHR confirmed by 2 assessments >=2 weeks apart; increasing WBC defined as doubling of WBC over a period of >=1 month with second WBC >20*10^9/L confirmed >=1 week later. Percentage of subjects with PFS/death events based on cumulative incidence method adjusting for competing event of treatment discontinuation without event. The full analysis set from B1871006 included all dosed subjects from the study B1871006.

End point type	Primary

End point timeframe:

Year 10

Notes:

[16] - 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 endpoint reports data for B1871006 subjects.

[17] - 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: The endpoint reports data for B1871006 subjects.

End point values	Bosutinib, CP2L	Bosutinib, CP3L/CP4L	Bosutinib, ADV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	119	167	
Units: percentage of subjects				
number (confidence interval 95%)	23.9 (19.5 to 29.5)	26.9 (20.0 to 36.2)	55.7 (48.6 to 63.8)	

Statistical analyses

No statistical analyses for this end point

Primary: Cumulative Incidence of Rate of Transformation to Accelerated Phase (AP) or Blast Phase (BP) at Year 10: B1871006 Subjects

End point title	Cumulative Incidence of Rate of Transformation to Accelerated Phase (AP) or Blast Phase (BP) at Year 10: B1871006 Subjects[18][19]

End point description:

Time to transformation was defined as the time from first dose in the parent study to the first date of confirmed transformation to AP or BP. Confirmed transformation was defined as 2 consecutive assessments at least 1 week apart or 1 assessment confirmed by progression of disease or death. For subjects without transformation, censorship was at the last evaluation date. Percentage of subjects with time to transformation to AP/BP was reported based on cumulative incidence method adjusting for the competing risk of treatment discontinuation without the event. The full analysis set from B1871006 included all dosed subjects from the study B1871006. For "Bosutinib ADV" reporting arm, data was analysed for subjects with AP who had BP transformation only.

End point type	Primary

End point timeframe:

Year 10

Notes:

[18] - 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 endpoint reports data for B1871006 subjects.

[19] - 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: The endpoint reports data for B1871006 subjects.

End point values	Bosutinib, CP2L	Bosutinib, CP3L/CP4L	Bosutinib, ADV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	119	79	
Units: percentage of subjects				
number (confidence interval 95%)	5.3 (3.2 to 8.6)	4.2 (1.8 to 9.9)	3.8 (1.3 to 11.5)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug and up to 30 days after last dose (up to approximately 14 years)

Adverse event reporting additional description:

The total number of deaths during study, from randomisation (B1871008)/first dose (B1871006) and up to end of the study are reported for all treated subjects and includes deaths which occurred after 30 days post last study drug dose. SAEs and other AEs: Analysis performed on safety set. Combined data from parent studies and this study reported.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Bosutinib, CP1L

Reporting group description:

Subjects from B1871008 with Philadelphia chromosome-positive (Ph+) chronic phase 1st line (CP1L) chronic myeloid leukemia (CML).

Reporting group title	Bosutinib, CP2L

Reporting group description:

Subjects from B1871006 with Ph+ chronic phase 2nd line (CP2L) CML who were resistant or intolerant to imatinib.

Reporting group title	Bosutinib, CP3L/CP4L

Reporting group description:

Subjects from B1871006 with Ph+ chronic phase 3rd line (CP3L)/4th line (CP4L) CML who were resistant or intolerant to imatinib and resistant or intolerant to dasatinib and/or nilotinib.

Reporting group title	Bosutinib, ADV

Reporting group description:

Subjects from B1871006 with Ph+ accelerated phase (AP), blast phase (BP) CML and Ph+ acute lymphoblastic leukemia (ALL) and resistant or intolerant to imatinib only or resistant and intolerant to imatinib and at least 1 additional tyrosine kinase inhibitor (TKI) including dasatinib and/or nilotinib.

Reporting group title	Bosutinib, Total

Reporting group description:

Subjects from B1871008 CP1L cohort and B1871006 CP2L, CP3L/CP4L and ADV cohorts.

Serious adverse events	Bosutinib, CP1L	Bosutinib, CP2L	Bosutinib, CP3L/CP4L
Total subjects affected by serious adverse events			
subjects affected / exposed	102 / 248 (41.13%)	124 / 284 (43.66%)	44 / 119 (36.97%)
number of deaths (all causes)	23	55	30
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Blast cell crisis			
subjects affected / exposed	1 / 248 (0.40%)	3 / 284 (1.06%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 2	1 / 1	0 / 0

Adenocarcinoma gastric			
subjects affected / exposed	3 / 248 (1.21%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	1 / 248 (0.40%)	2 / 284 (0.70%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blast crisis in myelogenous leukaemia			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	2 / 284 (0.70%)	0 / 119 (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 myeloid leukaemia			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angiomyolipoma			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder squamous cell carcinoma stage unspecified			

subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Bowen's disease			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Central nervous system leukaemia			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangiocarcinoma			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Chronic myelomonocytic leukaemia			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Follicle centre lymphoma, follicular grade I, II, III			

subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Keratoacanthoma			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal neoplasm			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipoma			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Lung adenocarcinoma			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Malignant melanoma			

subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Melanocytic naevus			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 skin			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Non-small cell lung cancer			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraproteinaemia			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Uterine leiomyoma			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.40%)	2 / 284 (0.70%)	0 / 119 (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
Hypotension			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Haemorrhage			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Hypertensive crisis			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Surgical and medical procedures			
Allogenic bone marrow transplantation therapy			

subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cyst removal			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Knee arthroplasty			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	2 / 248 (0.81%)	0 / 284 (0.00%)	0 / 119 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	8 / 248 (3.23%)	8 / 284 (2.82%)	2 / 119 (1.68%)
occurrences causally related to treatment / all	1 / 8	8 / 15	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	0 / 248 (0.00%)	3 / 284 (1.06%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 1
Chest pain			
subjects affected / exposed	1 / 248 (0.40%)	3 / 284 (1.06%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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	0 / 248 (0.00%)	4 / 284 (1.41%)	0 / 119 (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
Pain			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Chills			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Death			
subjects affected / exposed	1 / 248 (0.40%)	1 / 284 (0.35%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 3	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Oedema			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adhesion			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Malaise			

subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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 / 1
Swelling			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 248 (0.40%)	1 / 284 (0.35%)	0 / 119 (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
Anaphylactic shock			
subjects affected / exposed	2 / 248 (0.81%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Social circumstances			

Pregnancy of partner			
subjects affected / exposed	2 / 248 (0.81%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 248 (0.00%)	2 / 284 (0.70%)	0 / 119 (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
Breast hyperplasia			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Metrorrhagia			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic pain			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	12 / 248 (4.84%)	15 / 284 (5.28%)	8 / 119 (6.72%)
occurrences causally related to treatment / all	13 / 16	7 / 22	6 / 10
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 248 (0.40%)	7 / 284 (2.46%)	3 / 119 (2.52%)
occurrences causally related to treatment / all	0 / 1	1 / 13	4 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 248 (0.40%)	2 / 284 (0.70%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	1 / 1	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 hypertension			
subjects affected / exposed	3 / 248 (1.21%)	1 / 284 (0.35%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	3 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Acute pulmonary oedema			
subjects affected / exposed	2 / 248 (0.81%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 248 (0.00%)	2 / 284 (0.70%)	0 / 119 (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 obstructive pulmonary disease			
subjects affected / exposed	1 / 248 (0.40%)	1 / 284 (0.35%)	0 / 119 (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
Interstitial lung disease			
subjects affected / exposed	2 / 248 (0.81%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	1 / 248 (0.40%)	1 / 284 (0.35%)	0 / 119 (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
Pleuritic pain			
subjects affected / exposed	1 / 248 (0.40%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiectasis			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Bronchitis chronic			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			

subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 arrest			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Vocal cord polyp			

subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Anxiety			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Completed suicide			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Confusional state			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Depression			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Disorientation			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Dissociative disorder			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Hallucination			

subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Hallucination, visual			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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			
Cholelithiasis			
subjects affected / exposed	2 / 248 (0.81%)	4 / 284 (1.41%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Gallbladder disorder			
subjects affected / exposed	0 / 248 (0.00%)	2 / 284 (0.70%)	0 / 119 (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
Bile duct stone			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis chronic			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Drug-induced liver injury			

subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder polyp			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Perforation bile duct			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	8 / 248 (3.23%)	1 / 284 (0.35%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	12 / 14	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 248 (1.61%)	1 / 284 (0.35%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	4 / 4	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	1 / 248 (0.40%)	1 / 284 (0.35%)	0 / 119 (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
Blood creatinine increased			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Lipase increased			

subjects affected / exposed	1 / 248 (0.40%)	1 / 284 (0.35%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amylase increased			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 creatine phosphokinase increased			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 lactate dehydrogenase increased			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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 pressure increased			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Hepatic enzyme increased			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Liver function test increased			

subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Transaminases increased			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Weight decreased			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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			
Contusion			
subjects affected / exposed	1 / 248 (0.40%)	2 / 284 (0.70%)	0 / 119 (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
Facial bones fracture			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Road traffic accident			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Subdural haematoma			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 248 (0.00%)	2 / 284 (0.70%)	0 / 119 (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 injury			

subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Exposure during pregnancy			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to anastomose			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Fall			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Fibula fracture			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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 stoma complication			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 limb fracture			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Muscle injury			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
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 complication			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 procedural haematoma			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 procedural haematuria			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Rib fracture			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
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 laceration			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Skull fracture			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Subdural haemorrhage			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Transfusion reaction			

subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic lung injury			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Congenital, familial and genetic disorders			
Cytogenetic abnormality			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocele			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	6 / 248 (2.42%)	5 / 284 (1.76%)	2 / 119 (1.68%)
occurrences causally related to treatment / all	4 / 8	4 / 6	2 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	2 / 248 (0.81%)	6 / 284 (2.11%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	2 / 4	0 / 11	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 0

Atrial fibrillation			
subjects affected / exposed	1 / 248 (0.40%)	4 / 284 (1.41%)	3 / 119 (2.52%)
occurrences causally related to treatment / all	0 / 1	0 / 5	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	3 / 248 (1.21%)	2 / 284 (0.70%)	2 / 119 (1.68%)
occurrences causally related to treatment / all	0 / 3	1 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	1 / 248 (0.40%)	3 / 284 (1.06%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Cardiac failure			
subjects affected / exposed	0 / 248 (0.00%)	4 / 284 (1.41%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	1 / 8	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pericarditis			
subjects affected / exposed	2 / 248 (0.81%)	1 / 284 (0.35%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	2 / 2	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 248 (0.00%)	3 / 284 (1.06%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	1 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	3 / 119 (2.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Left ventricular dysfunction			
subjects affected / exposed	0 / 248 (0.00%)	2 / 284 (0.70%)	0 / 119 (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
Angina unstable			

subjects affected / exposed	0 / 248 (0.00%)	2 / 284 (0.70%)	0 / 119 (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
Pericardial haemorrhage			
subjects affected / exposed	0 / 248 (0.00%)	2 / 284 (0.70%)	0 / 119 (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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 coronary syndrome			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Aortic valve stenosis			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (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 / 0
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Bradycardia			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Bundle branch block right			

subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Cardiac disorder			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 failure acute			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Cardiorenal syndrome			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Coronary artery stenosis			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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	3 / 248 (1.21%)	1 / 284 (0.35%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	1 / 3	0 / 0	0 / 0
Extrasystoles			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Hypertensive cardiomyopathy			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Palpitations			

subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuropericarditis			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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	3 / 248 (1.21%)	0 / 284 (0.00%)	2 / 119 (1.68%)
occurrences causally related to treatment / all	2 / 4	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 248 (0.40%)	4 / 284 (1.41%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	2 / 248 (0.81%)	1 / 284 (0.35%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 248 (0.00%)	2 / 284 (0.70%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cerebral infarction			

subjects affected / exposed	0 / 248 (0.00%)	2 / 284 (0.70%)	0 / 119 (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
Cerebellar infarction			
subjects affected / exposed	0 / 248 (0.00%)	2 / 284 (0.70%)	0 / 119 (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
Dizziness			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	2 / 248 (0.81%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid arteriosclerosis			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Carpal tunnel syndrome			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis post varicella			

subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Hemiparesis			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculopathy			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Trigeminal neuralgia			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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	6 / 248 (2.42%)	5 / 284 (1.76%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	9 / 9	5 / 10	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	6 / 248 (2.42%)	3 / 284 (1.06%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	2 / 6	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			

subjects affected / exposed	2 / 248 (0.81%)	0 / 284 (0.00%)	4 / 119 (3.36%)
occurrences causally related to treatment / all	1 / 2	0 / 0	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Hyperleukocytosis			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Granulocytopenia			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Iron deficiency anaemia			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Leukopenia			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Pancytopenia			

subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Vestibular disorder			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Eye disorders			
Glaucoma			
subjects affected / exposed	1 / 248 (0.40%)	1 / 284 (0.35%)	0 / 119 (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
Cataract			
subjects affected / exposed	1 / 248 (0.40%)	1 / 284 (0.35%)	0 / 119 (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
Visual impairment			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Diplopia			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinopathy			

subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Retinopathy hypertensive			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitreous haemorrhage			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 disorders			
Diarrhoea			
subjects affected / exposed	9 / 248 (3.63%)	8 / 284 (2.82%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	11 / 12	7 / 9	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	3 / 248 (1.21%)	3 / 284 (1.06%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	2 / 3	2 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	3 / 248 (1.21%)	2 / 284 (0.70%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	3 / 248 (1.21%)	1 / 284 (0.35%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	1 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			

subjects affected / exposed	1 / 248 (0.40%)	3 / 284 (1.06%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Inguinal hernia			
subjects affected / exposed	0 / 248 (0.00%)	3 / 284 (1.06%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	2 / 248 (0.81%)	1 / 284 (0.35%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 248 (0.00%)	2 / 284 (0.70%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 ulcer			
subjects affected / exposed	2 / 248 (0.81%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorder			

subjects affected / exposed	2 / 248 (0.81%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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	0 / 248 (0.00%)	2 / 284 (0.70%)	0 / 119 (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
Toothache			
subjects affected / exposed	0 / 248 (0.00%)	2 / 284 (0.70%)	0 / 119 (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 adhesions			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Ascites			

subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Colitis ischaemic			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Dental caries			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Enteritis			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Epigastric discomfort			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecaloma			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 haemorrhage			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 haemorrhagic			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Gastrointestinal necrosis			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Intestinal haemorrhage			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
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 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Large intestinal stenosis			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Melaena			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Mesenteric artery embolism			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Oesophageal perforation			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal polyp			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Retroperitoneal haemorrhage			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Umbilical hernia			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 248 (0.40%)	8 / 284 (2.82%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	1 / 1	8 / 8	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	2 / 119 (1.68%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angioedema			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Circumoral oedema			

subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Dermatitis			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Skin disorder			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Skin lesion			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 and urinary disorders			
Acute kidney injury			
subjects affected / exposed	5 / 248 (2.02%)	6 / 284 (2.11%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 5	1 / 10	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Renal failure			
subjects affected / exposed	1 / 248 (0.40%)	2 / 284 (0.70%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	1 / 1	0 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			

subjects affected / exposed	1 / 248 (0.40%)	2 / 284 (0.70%)	0 / 119 (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
Calculus urinary			
subjects affected / exposed	2 / 248 (0.81%)	0 / 284 (0.00%)	0 / 119 (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
Calculus bladder			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
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 kidney disease			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Cystitis haemorrhagic			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
End stage renal disease			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 artery stenosis			

subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 disorder			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 retention			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Thyroid mass			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 248 (0.81%)	2 / 284 (0.70%)	2 / 119 (1.68%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gouty arthritis			
subjects affected / exposed	1 / 248 (0.40%)	1 / 284 (0.35%)	0 / 119 (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
Intervertebral disc disorder			
subjects affected / exposed	2 / 248 (0.81%)	0 / 284 (0.00%)	0 / 119 (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
Osteoarthritis			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	1 / 248 (0.40%)	1 / 284 (0.35%)	0 / 119 (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
Arthralgia			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Bone cyst			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 pain			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint range of motion decreased			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mandibular mass			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Musculoskeletal stiffness			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Myalgia			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Neck pain			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Osteochondrosis			

subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Osteonecrosis			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 in extremity			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Rotator cuff syndrome			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal stenosis			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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	10 / 248 (4.03%)	15 / 284 (5.28%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	2 / 14	3 / 18	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 1
Sepsis			
subjects affected / exposed	1 / 248 (0.40%)	4 / 284 (1.41%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cellulitis			

subjects affected / exposed	3 / 248 (1.21%)	3 / 284 (1.06%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 5	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 248 (0.81%)	4 / 284 (1.41%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	2 / 248 (0.81%)	3 / 284 (1.06%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	3 / 248 (1.21%)	3 / 284 (1.06%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 4	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 248 (0.00%)	4 / 284 (1.41%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 248 (0.40%)	2 / 284 (0.70%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 248 (0.40%)	1 / 284 (0.35%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	1 / 248 (0.40%)	2 / 284 (0.70%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			

subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	2 / 284 (0.70%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 248 (0.40%)	2 / 284 (0.70%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Device related infection			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Erysipelas			
subjects affected / exposed	0 / 248 (0.00%)	2 / 284 (0.70%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 248 (0.00%)	2 / 284 (0.70%)	0 / 119 (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
Infectious pleural effusion			
subjects affected / exposed	1 / 248 (0.40%)	1 / 284 (0.35%)	0 / 119 (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
Large intestine infection			

subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Pharyngitis			
subjects affected / exposed	1 / 248 (0.40%)	1 / 284 (0.35%)	0 / 119 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 248 (0.00%)	2 / 284 (0.70%)	0 / 119 (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
Septic shock			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Sinusitis			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 bacteraemia			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 abscess			
subjects affected / exposed	1 / 248 (0.40%)	1 / 284 (0.35%)	0 / 119 (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
Tooth infection			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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 tract infection bacterial			

subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Arthritis bacterial			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Arthritis infective			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Bacterial sepsis			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Catheter bacteraemia			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 of male external genital organ			

subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Clostridium difficile infection			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Cystitis			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Dengue fever			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis infected			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Diverticulitis			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eczema infected			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal sepsis			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis infectious			

subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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 bacteraemia			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 infection			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Gingival abscess			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Hepatitis A			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Infected dermal cyst			

subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Malaria			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Meningitis			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngotonsillitis			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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 bacterial			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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 procedural infection			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Pseudomonal sepsis			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Salmonella bacteraemia			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Salmonellosis			

subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Staphylococcal sepsis			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal sepsis			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Subcutaneous abscess			
subjects affected / exposed	1 / 248 (0.40%)	0 / 284 (0.00%)	0 / 119 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 248 (0.81%)	2 / 284 (0.70%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.40%)	1 / 284 (0.35%)	0 / 119 (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
Fluid retention			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			

subjects affected / exposed	0 / 248 (0.00%)	2 / 284 (0.70%)	0 / 119 (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
Acidosis			
subjects affected / exposed	0 / 248 (0.00%)	0 / 284 (0.00%)	0 / 119 (0.00%)
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 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Hyperglycaemia			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Hypophosphataemia			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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
Hypovolaemia			
subjects affected / exposed	0 / 248 (0.00%)	1 / 284 (0.35%)	0 / 119 (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, ADV	Bosutinib, Total	
Total subjects affected by serious adverse events			
subjects affected / exposed	98 / 167 (58.68%)	368 / 818 (44.99%)	
number of deaths (all causes)	98	206	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Blast cell crisis			
subjects affected / exposed	2 / 167 (1.20%)	6 / 818 (0.73%)	
occurrences causally related to treatment / all	0 / 2	1 / 7	
deaths causally related to treatment / all	0 / 1	1 / 4	

Adenocarcinoma gastric			
subjects affected / exposed	0 / 167 (0.00%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Basal cell carcinoma			
subjects affected / exposed	0 / 167 (0.00%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blast crisis in myelogenous leukaemia			
subjects affected / exposed	3 / 167 (1.80%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 167 (0.60%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myeloid leukaemia			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Squamous cell carcinoma			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angiomyolipoma			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anogenital warts			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder squamous cell carcinoma stage unspecified			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen's disease			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system leukaemia			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chloroma			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiocarcinoma			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Chronic myelomonocytic leukaemia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer metastatic			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Follicle centre lymphoma, follicular grade I, II, III			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratoacanthoma			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal neoplasm			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukaemia			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Lipoma			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Melanocytic naevus			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm prostate			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm skin			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraproteinaemia			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Uterine leiomyoma			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			

subjects affected / exposed	1 / 167 (0.60%)	4 / 818 (0.49%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	2 / 167 (1.20%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic stenosis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Allogenic bone marrow transplantation therapy			

subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cyst removal			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee arthroplasty			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	11 / 167 (6.59%)	29 / 818 (3.55%)	
occurrences causally related to treatment / all	5 / 17	14 / 43	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	8 / 167 (4.79%)	12 / 818 (1.47%)	
occurrences causally related to treatment / all	0 / 12	0 / 16	
deaths causally related to treatment / all	0 / 8	0 / 12	
Chest pain			
subjects affected / exposed	4 / 167 (2.40%)	8 / 818 (0.98%)	
occurrences causally related to treatment / all	0 / 4	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	6 / 167 (3.59%)	7 / 818 (0.86%)	
occurrences causally related to treatment / all	1 / 9	1 / 10	
deaths causally related to treatment / all	0 / 3	0 / 3	

Asthenia			
subjects affected / exposed	1 / 167 (0.60%)	5 / 818 (0.61%)	
occurrences causally related to treatment / all	1 / 1	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	2 / 167 (1.20%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 4	
Multiple organ dysfunction syndrome			
subjects affected / exposed	2 / 167 (1.20%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 3	
Oedema			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adhesion			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adverse drug reaction			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			

subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 2	
Swelling			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 167 (0.60%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	1 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic shock			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			

Pregnancy of partner			
subjects affected / exposed	0 / 167 (0.00%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast hyperplasia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical dysplasia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysfunctional uterine bleeding			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metrorrhagia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic pain			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal haemorrhage			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	8 / 167 (4.79%)	43 / 818 (5.26%)	
occurrences causally related to treatment / all	9 / 11	35 / 59	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dyspnoea			
subjects affected / exposed	5 / 167 (2.99%)	16 / 818 (1.96%)	
occurrences causally related to treatment / all	1 / 6	6 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	2 / 167 (1.20%)	6 / 818 (0.73%)	
occurrences causally related to treatment / all	0 / 2	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	5 / 167 (2.99%)	6 / 818 (0.73%)	
occurrences causally related to treatment / all	1 / 6	1 / 7	
deaths causally related to treatment / all	0 / 3	0 / 3	
Pulmonary hypertension			
subjects affected / exposed	0 / 167 (0.00%)	4 / 818 (0.49%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 167 (0.60%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute pulmonary oedema			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Asthma			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic pain			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiectasis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis chronic			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			

subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Organising pneumonia			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory arrest			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord polyp			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Confusional state			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dissociative disorder			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination, visual			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 167 (0.60%)	7 / 818 (0.86%)	
occurrences causally related to treatment / all	0 / 1	2 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 167 (0.60%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	2 / 167 (1.20%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder disorder			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder polyp			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perforation bile duct			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 167 (0.00%)	9 / 818 (1.10%)	
occurrences causally related to treatment / all	0 / 0	13 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 167 (0.00%)	5 / 818 (0.61%)	
occurrences causally related to treatment / all	0 / 0	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipase increased			

subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amylase increased			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose increased			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure increased			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraocular pressure increased			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test increased			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 167 (0.00%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Upper limb fracture			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal injury			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exposure during pregnancy			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to anastomose			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal stoma complication			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle injury			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematoma			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematuria			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural swelling			

subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural haemorrhage			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Subdural haemorrhage			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth fracture			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transfusion reaction			

subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic lung injury			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound haematoma			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Cytogenetic abnormality			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocele			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	2 / 167 (1.20%)	15 / 818 (1.83%)	
occurrences causally related to treatment / all	3 / 3	13 / 19	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure congestive			
subjects affected / exposed	1 / 167 (0.60%)	10 / 818 (1.22%)	
occurrences causally related to treatment / all	0 / 2	3 / 18	
deaths causally related to treatment / all	0 / 1	0 / 4	

Atrial fibrillation			
subjects affected / exposed	1 / 167 (0.60%)	9 / 818 (1.10%)	
occurrences causally related to treatment / all	0 / 1	1 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 167 (0.60%)	8 / 818 (0.98%)	
occurrences causally related to treatment / all	0 / 2	2 / 9	
deaths causally related to treatment / all	0 / 1	0 / 1	
Acute myocardial infarction			
subjects affected / exposed	2 / 167 (1.20%)	7 / 818 (0.86%)	
occurrences causally related to treatment / all	0 / 2	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 2	
Cardiac failure			
subjects affected / exposed	1 / 167 (0.60%)	6 / 818 (0.73%)	
occurrences causally related to treatment / all	0 / 1	2 / 10	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pericarditis			
subjects affected / exposed	1 / 167 (0.60%)	5 / 818 (0.61%)	
occurrences causally related to treatment / all	1 / 1	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 167 (0.00%)	4 / 818 (0.49%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 167 (0.60%)	4 / 818 (0.49%)	
occurrences causally related to treatment / all	1 / 1	1 / 5	
deaths causally related to treatment / all	1 / 1	1 / 3	
Left ventricular dysfunction			
subjects affected / exposed	1 / 167 (0.60%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			

subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial haemorrhage			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	2 / 167 (1.20%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bundle branch block right			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorder			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiorenal syndrome			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 167 (0.00%)	4 / 818 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	1 / 3	
Extrasystoles			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive cardiomyopathy			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Palpitations			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuropericarditis			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 167 (4.79%)	13 / 818 (1.59%)	
occurrences causally related to treatment / all	0 / 9	2 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 167 (0.00%)	5 / 818 (0.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 167 (0.60%)	4 / 818 (0.49%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Subarachnoid haemorrhage			
subjects affected / exposed	2 / 167 (1.20%)	4 / 818 (0.49%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 2	
Cerebral haemorrhage			
subjects affected / exposed	2 / 167 (1.20%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 2	0 / 3	
Cerebral infarction			

subjects affected / exposed	1 / 167 (0.60%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 2	1 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cerebellar infarction			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorder			
subjects affected / exposed	2 / 167 (1.20%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid arteriosclerosis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis post varicella			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraventricular haemorrhage			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Ischaemic stroke			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monoparesis			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinson's disease			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculopathy			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Speech disorder			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigeminal neuralgia			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	8 / 167 (4.79%)	20 / 818 (2.44%)	
occurrences causally related to treatment / all	17 / 24	32 / 44	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	6 / 167 (3.59%)	15 / 818 (1.83%)	
occurrences causally related to treatment / all	0 / 7	2 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	8 / 167 (4.79%)	9 / 818 (1.10%)	
occurrences causally related to treatment / all	1 / 10	2 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			

subjects affected / exposed	2 / 167 (1.20%)	8 / 818 (0.98%)	
occurrences causally related to treatment / all	1 / 2	5 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	3 / 167 (1.80%)	4 / 818 (0.49%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperleukocytosis			
subjects affected / exposed	2 / 167 (1.20%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Granulocytopenia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukostasis syndrome			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Lymphadenopathy			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			

subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenomegaly			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular disorder			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Glaucoma			
subjects affected / exposed	1 / 167 (0.60%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual impairment			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplopia			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinopathy			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinopathy hypertensive			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 167 (2.40%)	22 / 818 (2.69%)	
occurrences causally related to treatment / all	2 / 4	21 / 26	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	5 / 167 (2.99%)	11 / 818 (1.34%)	
occurrences causally related to treatment / all	1 / 7	5 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	5 / 167 (2.99%)	10 / 818 (1.22%)	
occurrences causally related to treatment / all	3 / 5	5 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	6 / 167 (3.59%)	8 / 818 (0.98%)	
occurrences causally related to treatment / all	3 / 6	3 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 167 (0.60%)	6 / 818 (0.73%)	
occurrences causally related to treatment / all	2 / 2	3 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			

subjects affected / exposed	1 / 167 (0.60%)	5 / 818 (0.61%)	
occurrences causally related to treatment / all	0 / 2	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	3 / 167 (1.80%)	4 / 818 (0.49%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Inguinal hernia			
subjects affected / exposed	0 / 167 (0.00%)	4 / 818 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 167 (0.60%)	4 / 818 (0.49%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Colitis			
subjects affected / exposed	0 / 167 (0.00%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 167 (0.60%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			

subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toothache			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal adhesions			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal distension			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain lower			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dental caries			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epigastric discomfort			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food poisoning			

subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis haemorrhagic			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal necrosis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haemorrhage			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Large intestinal stenosis			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Melaena			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric artery embolism			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal perforation			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal polyp			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haemorrhage			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 167 (0.60%)	11 / 818 (1.34%)	
occurrences causally related to treatment / all	0 / 1	10 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	1 / 167 (0.60%)	4 / 818 (0.49%)	
occurrences causally related to treatment / all	1 / 1	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioedema			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circumoral oedema			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythema multiforme			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin disorder			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin lesion			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 167 (1.80%)	15 / 818 (1.83%)	
occurrences causally related to treatment / all	0 / 3	1 / 19	
deaths causally related to treatment / all	0 / 0	0 / 2	
Renal failure			
subjects affected / exposed	1 / 167 (0.60%)	5 / 818 (0.61%)	
occurrences causally related to treatment / all	0 / 1	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			

subjects affected / exposed	0 / 167 (0.00%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus bladder			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis haemorrhagic			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
End stage renal disease			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prerenal failure			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery stenosis			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal disorder			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid mass			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 167 (0.00%)	6 / 818 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gouty arthritis			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone cyst			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin pain			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint range of motion decreased			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mandibular mass			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteochondrosis			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal stenosis			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	19 / 167 (11.38%)	44 / 818 (5.38%)	
occurrences causally related to treatment / all	2 / 26	7 / 58	
deaths causally related to treatment / all	0 / 3	0 / 7	
Sepsis			
subjects affected / exposed	6 / 167 (3.59%)	12 / 818 (1.47%)	
occurrences causally related to treatment / all	1 / 8	1 / 15	
deaths causally related to treatment / all	0 / 3	0 / 4	
Cellulitis			

subjects affected / exposed	1 / 167 (0.60%)	8 / 818 (0.98%)	
occurrences causally related to treatment / all	0 / 1	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 167 (0.60%)	7 / 818 (0.86%)	
occurrences causally related to treatment / all	0 / 1	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 167 (0.00%)	6 / 818 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 167 (0.00%)	6 / 818 (0.73%)	
occurrences causally related to treatment / all	0 / 0	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 167 (0.60%)	6 / 818 (0.73%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 167 (0.00%)	4 / 818 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 167 (0.00%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 167 (0.00%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			

subjects affected / exposed	3 / 167 (1.80%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	1 / 3	1 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Clostridium difficile colitis			
subjects affected / exposed	0 / 167 (0.00%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 167 (0.00%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine infection			

subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Sinusitis			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth infection			
subjects affected / exposed	1 / 167 (0.60%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			

subjects affected / exposed	2 / 167 (1.20%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain abscess			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter bacteraemia			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis of male external genital organ			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis infected			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema infected			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal sepsis			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Enterocolitis infectious			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal infection			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Gastrointestinal infection			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gingival abscess			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis A			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected dermal cyst			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaria			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal abscess			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia fungal			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pneumonia necrotising			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomembranous colitis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonal sepsis			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mycosis			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pyelonephritis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonella bacteraemia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonellosis			

subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 167 (1.80%)	8 / 818 (0.98%)	
occurrences causally related to treatment / all	1 / 3	1 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	3 / 167 (1.80%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Gout			
subjects affected / exposed	1 / 167 (0.60%)	3 / 818 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid retention			
subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			

subjects affected / exposed	0 / 167 (0.00%)	2 / 818 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acidosis			
subjects affected / exposed	1 / 167 (0.60%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	1 / 1	1 / 1	
Decreased appetite			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophosphataemia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 818 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Bosutinib, CP1L	Bosutinib, CP2L	Bosutinib, CP3L/CP4L
Total subjects affected by non-serious adverse events			
subjects affected / exposed	239 / 248 (96.37%)	283 / 284 (99.65%)	119 / 119 (100.00%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	90 / 248 (36.29%)	67 / 284 (23.59%)	19 / 119 (15.97%)
occurrences (all)	309	168	44
Aspartate aminotransferase			

increased			
subjects affected / exposed	74 / 248 (29.84%)	59 / 284 (20.77%)	10 / 119 (8.40%)
occurrences (all)	183	124	14
Lipase increased			
subjects affected / exposed	52 / 248 (20.97%)	29 / 284 (10.21%)	8 / 119 (6.72%)
occurrences (all)	128	62	20
Blood creatinine increased			
subjects affected / exposed	23 / 248 (9.27%)	36 / 284 (12.68%)	16 / 119 (13.45%)
occurrences (all)	59	60	26
Weight decreased			
subjects affected / exposed	16 / 248 (6.45%)	36 / 284 (12.68%)	7 / 119 (5.88%)
occurrences (all)	27	42	7
Amylase increased			
subjects affected / exposed	30 / 248 (12.10%)	18 / 284 (6.34%)	6 / 119 (5.04%)
occurrences (all)	82	35	7
Blood creatine phosphokinase increased			
subjects affected / exposed	23 / 248 (9.27%)	18 / 284 (6.34%)	2 / 119 (1.68%)
occurrences (all)	44	28	14
Blood alkaline phosphatase increased			
subjects affected / exposed	20 / 248 (8.06%)	10 / 284 (3.52%)	6 / 119 (5.04%)
occurrences (all)	34	13	8
Vascular disorders			
Hypertension			
subjects affected / exposed	24 / 248 (9.68%)	30 / 284 (10.56%)	10 / 119 (8.40%)
occurrences (all)	34	57	15
Nervous system disorders			
Headache			
subjects affected / exposed	41 / 248 (16.53%)	54 / 284 (19.01%)	31 / 119 (26.05%)
occurrences (all)	68	140	55
Dizziness			
subjects affected / exposed	25 / 248 (10.08%)	26 / 284 (9.15%)	18 / 119 (15.13%)
occurrences (all)	37	43	26
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	80 / 248 (32.26%)	117 / 284 (41.20%)	45 / 119 (37.82%)
occurrences (all)	239	551	192

Anaemia			
subjects affected / exposed	72 / 248 (29.03%)	87 / 284 (30.63%)	28 / 119 (23.53%)
occurrences (all)	178	290	56
Neutropenia			
subjects affected / exposed	35 / 248 (14.11%)	46 / 284 (16.20%)	23 / 119 (19.33%)
occurrences (all)	87	154	67
Leukopenia			
subjects affected / exposed	25 / 248 (10.08%)	37 / 284 (13.03%)	5 / 119 (4.20%)
occurrences (all)	49	106	14
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	50 / 248 (20.16%)	79 / 284 (27.82%)	17 / 119 (14.29%)
occurrences (all)	74	156	30
Fatigue			
subjects affected / exposed	42 / 248 (16.94%)	73 / 284 (25.70%)	27 / 119 (22.69%)
occurrences (all)	78	184	39
Asthenia			
subjects affected / exposed	26 / 248 (10.48%)	45 / 284 (15.85%)	10 / 119 (8.40%)
occurrences (all)	65	122	17
Oedema peripheral			
subjects affected / exposed	17 / 248 (6.85%)	32 / 284 (11.27%)	13 / 119 (10.92%)
occurrences (all)	32	53	20
Pain			
subjects affected / exposed	7 / 248 (2.82%)	22 / 284 (7.75%)	7 / 119 (5.88%)
occurrences (all)	10	34	16
Oedema			
subjects affected / exposed	15 / 248 (6.05%)	16 / 284 (5.63%)	4 / 119 (3.36%)
occurrences (all)	21	17	10
Chest pain			
subjects affected / exposed	7 / 248 (2.82%)	21 / 284 (7.39%)	4 / 119 (3.36%)
occurrences (all)	9	29	5
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	177 / 248 (71.37%)	244 / 284 (85.92%)	99 / 119 (83.19%)
occurrences (all)	786	2275	729
Nausea			

subjects affected / exposed	89 / 248 (35.89%)	132 / 284 (46.48%)	58 / 119 (48.74%)
occurrences (all)	174	394	152
Vomiting			
subjects affected / exposed	88 / 248 (35.48%)	106 / 284 (37.32%)	47 / 119 (39.50%)
occurrences (all)	172	293	90
Abdominal pain			
subjects affected / exposed	39 / 248 (15.73%)	77 / 284 (27.11%)	28 / 119 (23.53%)
occurrences (all)	72	168	70
Abdominal pain upper			
subjects affected / exposed	40 / 248 (16.13%)	59 / 284 (20.77%)	21 / 119 (17.65%)
occurrences (all)	59	157	97
Constipation			
subjects affected / exposed	18 / 248 (7.26%)	44 / 284 (15.49%)	16 / 119 (13.45%)
occurrences (all)	25	73	29
Dyspepsia			
subjects affected / exposed	22 / 248 (8.87%)	29 / 284 (10.21%)	12 / 119 (10.08%)
occurrences (all)	31	66	38
Toothache			
subjects affected / exposed	14 / 248 (5.65%)	19 / 284 (6.69%)	5 / 119 (4.20%)
occurrences (all)	18	27	7
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	32 / 248 (12.90%)	70 / 284 (24.65%)	26 / 119 (21.85%)
occurrences (all)	59	108	43
Dyspnoea			
subjects affected / exposed	25 / 248 (10.08%)	34 / 284 (11.97%)	13 / 119 (10.92%)
occurrences (all)	57	52	39
Pleural effusion			
subjects affected / exposed	26 / 248 (10.48%)	32 / 284 (11.27%)	20 / 119 (16.81%)
occurrences (all)	58	67	58
Oropharyngeal pain			
subjects affected / exposed	15 / 248 (6.05%)	37 / 284 (13.03%)	11 / 119 (9.24%)
occurrences (all)	17	47	20
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	65 / 248 (26.21%)	105 / 284 (36.97%)	34 / 119 (28.57%)
occurrences (all)	140	217	61
Pruritus			
subjects affected / exposed	20 / 248 (8.06%)	29 / 284 (10.21%)	20 / 119 (16.81%)
occurrences (all)	25	51	31
Dry skin			
subjects affected / exposed	10 / 248 (4.03%)	22 / 284 (7.75%)	8 / 119 (6.72%)
occurrences (all)	12	33	12
Psychiatric disorders			
Insomnia			
subjects affected / exposed	12 / 248 (4.84%)	10 / 284 (3.52%)	10 / 119 (8.40%)
occurrences (all)	16	11	14
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	32 / 248 (12.90%)	55 / 284 (19.37%)	21 / 119 (17.65%)
occurrences (all)	43	76	48
Back pain			
subjects affected / exposed	26 / 248 (10.48%)	43 / 284 (15.14%)	15 / 119 (12.61%)
occurrences (all)	34	64	36
Pain in extremity			
subjects affected / exposed	23 / 248 (9.27%)	35 / 284 (12.32%)	10 / 119 (8.40%)
occurrences (all)	35	59	24
Myalgia			
subjects affected / exposed	16 / 248 (6.45%)	26 / 284 (9.15%)	6 / 119 (5.04%)
occurrences (all)	19	37	7
Bone pain			
subjects affected / exposed	11 / 248 (4.44%)	20 / 284 (7.04%)	9 / 119 (7.56%)
occurrences (all)	14	25	12
Musculoskeletal pain			
subjects affected / exposed	12 / 248 (4.84%)	11 / 284 (3.87%)	12 / 119 (10.08%)
occurrences (all)	13	16	16
Muscle spasms			
subjects affected / exposed	14 / 248 (5.65%)	14 / 284 (4.93%)	8 / 119 (6.72%)
occurrences (all)	18	25	20
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	30 / 248 (12.10%)	40 / 284 (14.08%)	14 / 119 (11.76%)
occurrences (all)	78	56	19
Upper respiratory tract infection			
subjects affected / exposed	39 / 248 (15.73%)	32 / 284 (11.27%)	12 / 119 (10.08%)
occurrences (all)	73	55	25
Influenza			
subjects affected / exposed	26 / 248 (10.48%)	30 / 284 (10.56%)	13 / 119 (10.92%)
occurrences (all)	37	50	18
Urinary tract infection			
subjects affected / exposed	15 / 248 (6.05%)	31 / 284 (10.92%)	7 / 119 (5.88%)
occurrences (all)	28	52	7
Bronchitis			
subjects affected / exposed	17 / 248 (6.85%)	16 / 284 (5.63%)	7 / 119 (5.88%)
occurrences (all)	31	17	10
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	23 / 248 (9.27%)	41 / 284 (14.44%)	15 / 119 (12.61%)
occurrences (all)	34	61	22
Hypophosphataemia			
subjects affected / exposed	26 / 248 (10.48%)	12 / 284 (4.23%)	3 / 119 (2.52%)
occurrences (all)	69	23	5
Hypokalaemia			
subjects affected / exposed	10 / 248 (4.03%)	16 / 284 (5.63%)	5 / 119 (4.20%)
occurrences (all)	18	23	12

Non-serious adverse events	Bosutinib, ADV	Bosutinib, Total	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	164 / 167 (98.20%)	805 / 818 (98.41%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	17 / 167 (10.18%)	193 / 818 (23.59%)	
occurrences (all)	53	574	
Aspartate aminotransferase increased			
subjects affected / exposed	17 / 167 (10.18%)	160 / 818 (19.56%)	
occurrences (all)	42	363	
Lipase increased			

subjects affected / exposed	9 / 167 (5.39%)	98 / 818 (11.98%)	
occurrences (all)	19	229	
Blood creatinine increased			
subjects affected / exposed	10 / 167 (5.99%)	85 / 818 (10.39%)	
occurrences (all)	16	161	
Weight decreased			
subjects affected / exposed	9 / 167 (5.39%)	68 / 818 (8.31%)	
occurrences (all)	11	87	
Amylase increased			
subjects affected / exposed	5 / 167 (2.99%)	59 / 818 (7.21%)	
occurrences (all)	10	134	
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 167 (1.80%)	46 / 818 (5.62%)	
occurrences (all)	4	90	
Blood alkaline phosphatase increased			
subjects affected / exposed	9 / 167 (5.39%)	45 / 818 (5.50%)	
occurrences (all)	20	75	
Vascular disorders			
Hypertension			
subjects affected / exposed	11 / 167 (6.59%)	75 / 818 (9.17%)	
occurrences (all)	13	119	
Nervous system disorders			
Headache			
subjects affected / exposed	30 / 167 (17.96%)	156 / 818 (19.07%)	
occurrences (all)	44	307	
Dizziness			
subjects affected / exposed	21 / 167 (12.57%)	90 / 818 (11.00%)	
occurrences (all)	21	127	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	69 / 167 (41.32%)	311 / 818 (38.02%)	
occurrences (all)	333	1315	
Anaemia			
subjects affected / exposed	64 / 167 (38.32%)	251 / 818 (30.68%)	
occurrences (all)	204	728	
Neutropenia			

subjects affected / exposed	35 / 167 (20.96%)	139 / 818 (16.99%)	
occurrences (all)	117	425	
Leukopenia			
subjects affected / exposed	25 / 167 (14.97%)	92 / 818 (11.25%)	
occurrences (all)	63	232	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	59 / 167 (35.33%)	205 / 818 (25.06%)	
occurrences (all)	85	345	
Fatigue			
subjects affected / exposed	35 / 167 (20.96%)	177 / 818 (21.64%)	
occurrences (all)	46	347	
Asthenia			
subjects affected / exposed	19 / 167 (11.38%)	100 / 818 (12.22%)	
occurrences (all)	37	241	
Oedema peripheral			
subjects affected / exposed	18 / 167 (10.78%)	80 / 818 (9.78%)	
occurrences (all)	29	134	
Pain			
subjects affected / exposed	12 / 167 (7.19%)	48 / 818 (5.87%)	
occurrences (all)	17	77	
Oedema			
subjects affected / exposed	9 / 167 (5.39%)	44 / 818 (5.38%)	
occurrences (all)	9	57	
Chest pain			
subjects affected / exposed	11 / 167 (6.59%)	43 / 818 (5.26%)	
occurrences (all)	15	58	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	124 / 167 (74.25%)	644 / 818 (78.73%)	
occurrences (all)	414	4204	
Nausea			
subjects affected / exposed	78 / 167 (46.71%)	357 / 818 (43.64%)	
occurrences (all)	176	896	
Vomiting			

subjects affected / exposed	72 / 167 (43.11%)	313 / 818 (38.26%)	
occurrences (all)	139	694	
Abdominal pain			
subjects affected / exposed	34 / 167 (20.36%)	178 / 818 (21.76%)	
occurrences (all)	56	366	
Abdominal pain upper			
subjects affected / exposed	16 / 167 (9.58%)	136 / 818 (16.63%)	
occurrences (all)	31	344	
Constipation			
subjects affected / exposed	28 / 167 (16.77%)	106 / 818 (12.96%)	
occurrences (all)	42	169	
Dyspepsia			
subjects affected / exposed	12 / 167 (7.19%)	75 / 818 (9.17%)	
occurrences (all)	16	151	
Toothache			
subjects affected / exposed	3 / 167 (1.80%)	41 / 818 (5.01%)	
occurrences (all)	3	55	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	33 / 167 (19.76%)	161 / 818 (19.68%)	
occurrences (all)	56	266	
Dyspnoea			
subjects affected / exposed	30 / 167 (17.96%)	102 / 818 (12.47%)	
occurrences (all)	43	191	
Pleural effusion			
subjects affected / exposed	14 / 167 (8.38%)	92 / 818 (11.25%)	
occurrences (all)	25	208	
Oropharyngeal pain			
subjects affected / exposed	13 / 167 (7.78%)	76 / 818 (9.29%)	
occurrences (all)	21	105	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	52 / 167 (31.14%)	256 / 818 (31.30%)	
occurrences (all)	86	504	
Pruritus			

subjects affected / exposed	10 / 167 (5.99%)	79 / 818 (9.66%)	
occurrences (all)	23	130	
Dry skin			
subjects affected / exposed	4 / 167 (2.40%)	44 / 818 (5.38%)	
occurrences (all)	4	61	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	15 / 167 (8.98%)	47 / 818 (5.75%)	
occurrences (all)	22	63	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	24 / 167 (14.37%)	132 / 818 (16.14%)	
occurrences (all)	40	207	
Back pain			
subjects affected / exposed	16 / 167 (9.58%)	100 / 818 (12.22%)	
occurrences (all)	24	158	
Pain in extremity			
subjects affected / exposed	19 / 167 (11.38%)	87 / 818 (10.64%)	
occurrences (all)	31	149	
Myalgia			
subjects affected / exposed	14 / 167 (8.38%)	62 / 818 (7.58%)	
occurrences (all)	17	80	
Bone pain			
subjects affected / exposed	11 / 167 (6.59%)	51 / 818 (6.23%)	
occurrences (all)	13	64	
Musculoskeletal pain			
subjects affected / exposed	9 / 167 (5.39%)	44 / 818 (5.38%)	
occurrences (all)	14	59	
Muscle spasms			
subjects affected / exposed	7 / 167 (4.19%)	43 / 818 (5.26%)	
occurrences (all)	11	74	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	9 / 167 (5.39%)	93 / 818 (11.37%)	
occurrences (all)	11	164	
Upper respiratory tract infection			

subjects affected / exposed	10 / 167 (5.99%)	93 / 818 (11.37%)	
occurrences (all)	22	175	
Influenza			
subjects affected / exposed	6 / 167 (3.59%)	75 / 818 (9.17%)	
occurrences (all)	10	115	
Urinary tract infection			
subjects affected / exposed	2 / 167 (1.20%)	55 / 818 (6.72%)	
occurrences (all)	7	94	
Bronchitis			
subjects affected / exposed	6 / 167 (3.59%)	46 / 818 (5.62%)	
occurrences (all)	8	66	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	21 / 167 (12.57%)	100 / 818 (12.22%)	
occurrences (all)	32	149	
Hypophosphataemia			
subjects affected / exposed	10 / 167 (5.99%)	51 / 818 (6.23%)	
occurrences (all)	20	117	
Hypokalaemia			
subjects affected / exposed	10 / 167 (5.99%)	41 / 818 (5.01%)	
occurrences (all)	22	75	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 August 2016	Study objectives updated to fulfill a European Medicines Agency (EMA) post-approval requirement for the collection and analysis of the pharmacokinetics (PK) of bosutinib; Extension of bosutinib dosing of all eligible subjects to be studied for at least 10 years; Updated contraception language per current standard operating procedures (SOPs); Study procedures and efficacy assessment sections updated for consistency and allowance for local assessment of molecular response; Updated study conduct plans requiring mutational analysis of the BCR-ABL kinase domain to be performed by a central laboratory; Adverse event and exposure definitions updated per new protocol SOPs: Update to data analysis and statistical methods sections to define diarrhea and PK analyses.
07 November 2016	Update to exclude subjects from China from the pharmacokinetic (PK) analysis and the centralised testing for mutational analysis of the BCR-ABL kinase domain; Lifestyle guidelines and requirements for contraception updated throughout the protocol for consistency with updated Pfizer SOPs; Adverse event reporting and reporting requirements updated per Pfizer SOPs.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported