



Clinical trial results:

A Multicenter Phase 3 randomized, open-label study of bosutinib versus imatinib in adult subjects with newly diagnosed chronic phase chronic myelogenous leukemia (BFORE)

Summary

EudraCT number	2013-005101-31
Trial protocol	BE GB IT SE CZ HU SK FI NO ES DK NL PL FR
Global end of trial date	

Results information

Result version number	v1
This version publication date	28 July 2018
First version publication date	28 July 2018

Trial information

Trial identification

Sponsor protocol code	B1871053
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02130557
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 1-800-718-1021, ClinicalTrials.gov_inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 18007181021, 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	Interim
Date of interim/final analysis	20 April 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 August 2016
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the proportion of patients demonstrating Major Molecular Response (MMR) at 12 months (48 weeks) in the bosutinib arm with that of the imatinib arm in newly diagnosed Philadelphia chromosome positive (Ph+) chronic phase (CP) chronic myelogenous leukemia (CML) patients harboring b2a2 and/or b3a2 transcripts.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and The study was in compliance 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	15 July 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 7
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Canada: 18
Country: Number of subjects enrolled	Czech Republic: 11
Country: Number of subjects enrolled	Denmark: 6
Country: Number of subjects enrolled	Finland: 5
Country: Number of subjects enrolled	France: 18
Country: Number of subjects enrolled	Germany: 21
Country: Number of subjects enrolled	Hungary: 22
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Italy: 36
Country: Number of subjects enrolled	Korea, Republic of: 26
Country: Number of subjects enrolled	Mexico: 14
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Norway: 6
Country: Number of subjects enrolled	Poland: 25
Country: Number of subjects enrolled	Singapore: 17
Country: Number of subjects enrolled	Slovakia: 1

Country: Number of subjects enrolled	South Africa: 10
Country: Number of subjects enrolled	Spain: 35
Country: Number of subjects enrolled	Sweden: 15
Country: Number of subjects enrolled	Taiwan: 7
Country: Number of subjects enrolled	Thailand: 9
Country: Number of subjects enrolled	Ukraine: 81
Country: Number of subjects enrolled	United Kingdom: 42
Country: Number of subjects enrolled	United States: 88
Worldwide total number of subjects	536
EEA total number of subjects	257

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)	435
From 65 to 84 years	101
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Data reported was based on primary analysis date (11 August 2016).

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

Arm description:

Subjects with Philadelphia chromosome-positive chronic myeloid leukemia (CML) received bosutinib at a dose of 400 mg, orally once daily in the core treatment period of 12 months. Subjects who completed the core treatment period, entered into extension period and received same treatment.

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 400 mg, orally once daily.

Arm title	Imatinib
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Arm description:

Subjects with Philadelphia chromosome-positive CML received imatinib at a dose of 400 mg, orally once daily in the core treatment period of 12 months. Subjects who completed the core treatment period, entered into extension period and received same treatment.

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

Dosage and administration details:

Subjects received imatinib at a dose of 400 mg, orally once daily.

Number of subjects in period 1	Bosutinib	Imatinib
Started	268	268
Treated	268	265
mITT population	246	241
Completed	0	0
Not completed	268	268
Deceased	1	6
Consent withdrawn by subject	5	2
Ongoing	260	255
Lost to follow-up	2	2
Randomized, not treated	-	3

Baseline characteristics

Reporting groups

Reporting group title	Bosutinib
Reporting group description:	
Subjects with Philadelphia chromosome-positive chronic myeloid leukemia (CML) received bosutinib at a dose of 400 mg, orally once daily in the core treatment period of 12 months. Subjects who completed the core treatment period, entered into extension period and received same treatment.	
Reporting group title	Imatinib
Reporting group description:	
Subjects with Philadelphia chromosome-positive CML received imatinib at a dose of 400 mg, orally once daily in the core treatment period of 12 months. Subjects who completed the core treatment period, entered into extension period and received same treatment.	

Reporting group values	Bosutinib	Imatinib	Total
Number of subjects	268	268	536
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)	215	220	435
From 65-84 years	53	48	101
85 years and over	0	0	0
Age Continuous			
Units: years			
median	53.0	53.0	
full range (min-max)	18 to 84	19 to 84	-
Sex: Female, Male			
Units: Subjects			
Female	112	113	225
Male	156	155	311

End points

End points reporting groups

Reporting group title	Bosutinib
Reporting group description: Subjects with Philadelphia chromosome-positive chronic myeloid leukemia (CML) received bosutinib at a dose of 400 mg, orally once daily in the core treatment period of 12 months. Subjects who completed the core treatment period, entered into extension period and received same treatment.	
Reporting group title	Imatinib
Reporting group description: Subjects with Philadelphia chromosome-positive CML received imatinib at a dose of 400 mg, orally once daily in the core treatment period of 12 months. Subjects who completed the core treatment period, entered into extension period and received same treatment.	

Primary: Percentage of Subjects With Major Molecular Response (MMR) at Month 12

End point title	Percentage of Subjects With Major Molecular Response (MMR) at Month 12
End point description: MMR was defined as a ratio of breakpoint cluster region to abelson (Bcr-Abl/Abl) less than or equal to (\leq) 0.1 percent (%) on the international scale (IS) (greater than or equal to [\geq] 3 log reduction from standardized baseline in ratio of Bcr-Abl to Abl transcripts [\geq 3000 Abl required]) by quantitative reverse transcriptase polymerase chain reaction (RT-qPCR). Modified intent-to-treat (mITT) population included all randomized subjects with Philadelphia chromosome positive CML harboring the b2a2 and/or b3a2 transcript and baseline BCR-ABL copies greater than ($>$) 0 with study drug assignment designated according to initial randomization.	
End point type	Primary
End point timeframe: Month 12	

End point values	Bosutinib	Imatinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	241		
Units: percentage of subjects				
number (confidence interval 95%)	47.2 (40.9 to 53.4)	36.9 (30.8 to 43.0)		

Statistical analyses

Statistical analysis title	Bosutinib vs Imatinib
Statistical analysis description: 95% CI for the odds ratio adjusted for sokal risk group and region are based on asymptotic wald confidence limits.	
Comparison groups	Bosutinib v Imatinib

Number of subjects included in analysis	487
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.01 ^[1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.547
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.072
upper limit	2.233

Notes:

[1] - 1-sided p-value was based on a CMH test for general association between treatment and response with stratification by sokal risk group (low, intermediate, high) and region (1-3) as determined at time of randomization.

Secondary: Duration of Major Molecular Response (MMR)

End point title	Duration of Major Molecular Response (MMR)
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End point description:

Time from the first date of MMR until the date of the confirmed loss of MMR or censoring. Confirmed Loss of MMR was Bcr-Abl/Abl IS ratio >0.1% in association with a ≥ 5 -fold increase in Bcr-Abl/Abl IS ratio from the lowest value achieved up to that time-point confirmed by a second assessment at least 28 days later. Treatment discontinuation due to progressive disease(PD) or death due to PD within 28 days of last dose were considered confirmed loss of MMR. PD was defined as disease progression to accelerated phase(AP) or blast phase(BP) CML. Kaplan-meier analysis was used for determination of duration of MMR. Duration of response will be analyzed for responders only therefore duration of response will be excluded from the long-term family of secondary endpoints. mITT analysis set. N(overall number of subjects analyzed)=number of subjects evaluable for this endpoint. 99999 represents median and 95% C.I. could not be reached due to immaturity of events at the data cutoff date.

End point type	Secondary
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End point timeframe:

From the date of first MMR until the date of confirmed loss of MMR or censoring (up to 752 days)

End point values	Bosutinib	Imatinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	122		
Units: weeks				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Complete Cytogenetic Response (CCyR) by Month 12

End point title	Percentage of Subjects With Complete Cytogenetic Response (CCyR) by Month 12
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End point description:

Complete Cytogenetic Response (CCyR) was based on the prevalence of Philadelphia chromosome positive (Ph+) metaphases among cells in metaphase on a bone marrow (BM) aspirate. CCyR was achieved when there was 0 % Ph+ metaphases among cells in a BM sample when at least 20 metaphases from a BM sample were analyzed, or MMR if no BM was available. mITT population included all randomized subjects with Philadelphia chromosome positive CML harboring the b2a2 and/or b3a2 transcript and baseline BCR-ABL copies >0 with study drug assignment designated according to initial randomization.

End point type	Secondary
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End point timeframe:

up to Month 12

End point values	Bosutinib	Imatinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	241		
Units: percentage of subjects				
number (confidence interval 95%)	77.2 (72.0 to 82.5)	66.4 (60.4 to 72.4)		

Statistical analyses

Statistical analysis title	Bosutinib vs Imatinib
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Statistical analysis description:

95% CI for the odds ratio adjusted for sokal risk group and region are based on asymptotic wald confidence limits.

Comparison groups	Bosutinib v Imatinib
Number of subjects included in analysis	487
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0037 ^[2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.16
upper limit	2.61

Notes:

[2] - 1-sided p-value was based on a CMH test for general association between treatment and response with stratification by sokal risk group (low, intermediate, high) and region (1-3) as determined at time of randomization.

Secondary: Duration of Complete Cytogenetic Response (CCyR)

End point title	Duration of Complete Cytogenetic Response (CCyR)
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End point description:

It was defined as the time from the first date of CCyR until the date of the confirmed loss of CCyR or censoring. Confirmed Loss of CCyR was the presence of at least one Ph+ metaphase confirmed by a second assessment at least 28 days later. Treatment discontinuation due to PD or death due to PD within 28 days of last dose were considered confirmed loss of CCyR. PD was defined as disease

progression to accelerated phase or blast phase CML. Kaplan meier analysis was used for the determination of duration of CCyR. Duration of response will be analyzed for responders only therefore duration of response will be excluded from the long-term family of secondary endpoints. mITT analysis set. N=number of subjects evaluable for this endpoint. 99999 states that median and 95% C.I. was not estimable due to less number of subjects who had event.

End point type	Secondary
End point timeframe:	
From the date of first CCyR until the date of confirmed loss of CCyR or censoring (up to 752 days)	

End point values	Bosutinib	Imatinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	175		
Units: weeks				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Incidence of Event Free Survival (EFS) Events at Month 12

End point title	Cumulative Incidence of Event Free Survival (EFS) Events at Month 12
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End point description:

EFS was defined as the time from randomization to death due to any cause, transformation to AP or BP at any time, confirmed loss of complete hematologic response (CHR), confirmed loss of CCyR or censoring. Loss of CHR was defined as a hematologic assessment of non-CHR [chronic phase, AP, or BP] confirmed by 2 assessments at least 4 weeks apart). Loss of CCyR was defined as at least 1 Ph+ metaphase from analysis of <100 metaphases confirmed by a follow up cytogenetic analysis after 1 month. Cumulative incidence of EFS event at month 12 was adjusted for competing risk of treatment discontinuation without the event. The comparative analysis between two arms for this member of long term secondary family will be done at the end of the study. mITT population included all randomized subjects with Philadelphia chromosome positive CML harboring the b2a2 and/or b3a2 transcript and baseline BCR-ABL copies >0 with study drug assignment designated according to initial randomization.

End point type	Secondary
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End point timeframe:

Month 12

End point values	Bosutinib	Imatinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	241		
Units: percentage of subjects				
number (confidence interval 95%)	3.7 (1.8 to 6.7)	6.4 (3.7 to 10.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS) at Month 12

End point title	Overall survival (OS) at Month 12
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End point description:

OS was defined as the time (in months) from randomization to the occurrence of death due to any cause or censoring. Kaplan-meier analysis was used for determination of OS. The comparative analysis between the two arms for this member of the long-term secondary family will be done at the end of the study. mITT population included all randomized subjects with Philadelphia chromosome positive CML harboring the b2a2 and/or b3a2 transcript and baseline BCR-ABL copies >0 with study drug assignment designated according to initial randomization.

End point type	Secondary
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End point timeframe:

Month 12

End point values	Bosutinib	Imatinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	241		
Units: Months				
number (confidence interval 95%)	99.6 (97.0 to 99.9)	97.9 (95.0 to 99.1)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Summary of Trough Plasma Concentration by Complete Cytogenetic Response (CCyR)

End point title	Summary of Trough Plasma Concentration by Complete Cytogenetic Response (CCyR) ^[3]
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End point description:

CCyR is based on the prevalence of Ph+ metaphases among cells in metaphase on a BM aspirate. CCyR was achieved when there was 0 % Ph+ metaphases among cells in a BM sample when at least 20 metaphases from a BM sample were analyzed, or MMR if no BM was available. Trough plasma concentration of participants who had CCyR are presented in this endpoint. Pharmacokinetic (PK) population included all enrolled subjects who received at least 1 dose of bosutinib and had sufficient plasma results available. Here, "N" signifies number of subjects evaluable for this endpoint and "n" signifies subjects evaluable at specified time points only.

End point type	Other pre-specified
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End point timeframe:

Day 28, 56, 84

Notes:

[3] - 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: Descriptive analysis was planned to be reported for Bosutinib arm only.

End point values	Bosutinib			
Subject group type	Reporting group			
Number of subjects analysed	191			
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Day 28 (n =181)	71.282 (± 46.0545)			
Day 56 (n =184)	73.069 (± 45.1349)			
Day 84 (n =184)	83.973 (± 64.3206)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Summary of Trough Plasma Concentration by Major Molecular Response (MMR)

End point title	Summary of Trough Plasma Concentration by Major Molecular Response (MMR) ^[4]
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End point description:

MMR was defined as a ratio of Bcr-Abl/Abl $\leq 0.1\%$ on the international scale (≥ 3 log reduction from standardized baseline in ratio of Bcr-Abl to Abl transcripts) by quantitative RT-qPCR. Trough plasma concentration of subjects who had MMR are presented in this endpoint. PK population included all enrolled subjects who received at least 1 dose of bosutinib and had sufficient plasma results available. Here, "N" signifies number of subjects evaluable for this endpoint and "n" signifies subjects evaluable at specified time points only.

End point type	Other pre-specified
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End point timeframe:

Day 28, 56, 84

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Descriptive analysis was planned to be reported for Bosutinib arm only.

End point values	Bosutinib			
Subject group type	Reporting group			
Number of subjects analysed	141			
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 28 (n =140)	75.050 (± 51.9551)			
Day 56 (n =140)	78.437 (± 43.6019)			
Day 84 (n =141)	91.081 (± 72.1500)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Summary of Trough Plasma Concentration by Presence of Grade 1 or Higher Adverse Events (AEs)

End point title	Summary of Trough Plasma Concentration by Presence of Grade 1 or Higher Adverse Events (AEs) ^[5]
End point description:	
An AE was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. AE was assessed according to maximum severity grading based on National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0. Grade 1 =mild; Grade 2 =moderate; within normal limits, Grade 3 =severe or medically significant but not immediately life-threatening; Grade 4 =life-threatening or disabling; urgent intervention indicated; Grade 5 =death. Trough plasma concentration of subjects who had grade 1 or higher AE are presented in this endpoint. Data of plasma concentration is reported separately for each preferred term of AE. PK population included all enrolled subjects who received at least 1 dose of bosutinib and had sufficient plasma results available. Here,"N" signifies number of subjects evaluable for this endpoint and "n" signifies subjects evaluable at specified time points only.	
End point type	Other pre-specified
End point timeframe:	
Day 28, 56, 84	

Notes:

[5] - 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: Descriptive analysis was planned to be reported for Bosutinib arm only.

End point values	Bosutinib			
Subject group type	Reporting group			
Number of subjects analysed	177			
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 28: Diarrhea (n =177)	69.402 (± 55.5005)			
Day 28: Thrombocytopenia (n =60)	63.529 (± 40.9949)			
Day 28: Rash (n =84)	74.779 (± 60.6257)			
Day 28: Nausea (n =86)	66.011 (± 42.6437)			
Day 28: Vomiting (n =44)	71.684 (± 60.7208)			
Day 56: Diarrhea (n =172)	68.834 (± 42.6621)			
Day 56: Thrombocytopenia (n =61)	65.327 (± 43.2859)			
Day 56: Rash (n =84)	70.016 (± 38.7506)			
Day 56: Nausea (n =85)	61.626 (± 44.4007)			
Day 56: Vomiting (n =40)	65.980 (± 45.9064)			
Day 84: Diarrhea (n =165)	81.269 (± 64.6462)			
Day 84: Thrombocytopenia (n =63)	71.585 (± 33.6674)			
Day 84: Rash (n =85)	89.080 (± 69.5237)			
Day 84: Nausea (n =80)	77.702 (± 61.6179)			
Day 84: Vomiting (n =41)	86.949 (± 55.3041)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Summary of Trough Plasma Concentration by Presence of Grade 3 or Higher Adverse Events (AEs)

End point title	Summary of Trough Plasma Concentration by Presence of Grade 3 or Higher Adverse Events (AEs) ^[6]
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End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. AE was assessed according to maximum severity grading based on NCI CTCAE Version 4.0. Grade 1 =mild; Grade 2 =moderate; within normal limits, Grade 3 =severe or medically significant but not immediately life-threatening; Grade 4 =life-threatening or disabling; urgent intervention indicated; Grade 5 =death. Trough plasma concentration of participants who had grade 3 or higher AE are presented in this endpoint. Data of plasma concentration is reported separately for each preferred term of AE. PK population included all enrolled subjects who received at least 1 dose of bosutinib and had sufficient plasma results available. "N"=number of subjects evaluable for this endpoint and "n"=subjects evaluable at specified time points only. 99999 states that as only 1 subject was analyzed, standard deviation could not be calculated.

End point type	Other pre-specified
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End point timeframe:

Day 28, 56, 84

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Descriptive analysis was planned to be reported for Bosutinib arm only.

End point values	Bosutinib			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 28: Diarrhea (n =19)	87.769 (± 102.6181)			
Day 28: Thrombocytopenia (n =23)	49.220 (± 36.3461)			
Day 28: Rash (n =4)	71.150 (± 43.3246)			
Day 28: Vomiting (n =3)	14.663 (± 21.5799)			
Day 56: Diarrhea (n =16)	68.513 (± 45.2672)			
Day 56: Thrombocytopenia (n =24)	56.853 (± 34.3892)			
Day 56: Rash (n =4)	58.925 (± 18.8656)			
Day 56: Vomiting (n =1)	38.200 (± 99999)			
Day 84: Diarrhea (n =17)	76.782 (± 46.3006)			

Day 84: Thrombocytopenia (n =23)	67.623 (± 35.3084)			
Day 84: Rash (n =3)	83.967 (± 19.2542)			
Day 84: Vomiting (n =1)	12.400 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Vital Signs Abnormalities

End point title	Number of Subjects With Vital Signs Abnormalities
End point description:	
Criteria for vital signs abnormalities: systolic blood pressure (SBP) less than (<) 80 millimeter of mercury (mmHg), >210 mmHg; diastolic blood pressure (DBP) <40 mmHg, >130 mmHg; heart rate <40 beats per minute (bpm), >150 bpm; temperature <32 degree celsius, >40 degree celsius. Safety population included all subjects who received at least 1 dose of study medication with treatment assignments designated to actual study treatment received.	
End point type	Other pre-specified
End point timeframe:	
Baseline up to 752 days	

End point values	Bosutinib	Imatinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268	265		
Units: subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: 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
End point description:	
Laboratory parameters included hematological (haemoglobin, lymphocytes (absolute), neutrophils (absolute), platelets and leukocytes) and biochemistry (albumin, alanine aminotransferase, alkaline phosphatase, aspartate aminotransferase, amylase, bilirubin, creatinine kinase, calcium, creatinine, glucose, potassium, lipase, magnesium, phosphate, sodium, urate) parameters. Abnormalities in laboratory tests were graded by NCI CTCAE version 4.03 as Grade 1= mild; Grade 2= moderate; Grade 3= severe and Grade 4= life-threatening or disabling. Safety population included all subjects who received at least 1 dose of study medication with treatment assignments designated to actual study treatment received.	
End point type	Other pre-specified

End point timeframe:
Baseline up to 752 days

End point values	Bosutinib	Imatinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268	265		
Units: subjects				
Grade 1	15	17		
Grade 2	84	87		
Grade 3	114	116		
Grade 4	54	45		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Electrocardiogram (ECG) Abnormalities of Potential Clinical Concern

End point title	Number of Subjects With Electrocardiogram (ECG) Abnormalities of Potential Clinical Concern
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End point description:

Criteria for ECG abnormalities : heart rate: increase of >15 bpm from baseline value and ≥ 120 bpm, decrease of >15 bpm from baseline value and ≤ 45 bpm; PR interval: change of ≥ 20 msec from baseline value and ≥ 220 milliseconds (msec); QRS interval ≥ 120 msec; QTcB interval >500 msec, increase of >60 msec from baseline; QT interval using Fridericia's correction (QTcF) >500 msec, increase of >60 msec from baseline, ≤ 450 msec (Men) or ≤ 470 msec (Women), >450 msec (Men) or >470 msec (Women). Safety population included all subjects who received at least 1 dose of study medication with treatment assignments designated to actual study treatment received.

End point type	Other pre-specified
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End point timeframe:

Baseline up to 752 days

End point values	Bosutinib	Imatinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268	265		
Units: subjects	6	6		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Adverse Events (AEs) Leading to Study Drug Discontinuation

End point title	Number of Subjects With Adverse Events (AEs) Leading to Study Drug Discontinuation
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 population included all subjects who received at least 1 dose of study medication with treatment assignments designated to actual study treatment received.	
End point type	Other pre-specified
End point timeframe: Baseline up to 752 days	

End point values	Bosutinib	Imatinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268	265		
Units: subjects	38	28		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Treatment-Emergent Adverse Events By National Cancer Institute Common Terminology Criteria for AEs (NCI CTCAE) (Version 4.03)

End point title	Number of Subjects With Treatment-Emergent Adverse Events By National Cancer Institute Common Terminology Criteria for AEs (NCI CTCAE) (Version 4.03)
End point description: An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. AE was assessed according to severity grading based on NCI CTCAE version 4.03. Grade 1 =mild; Grade 2 =moderate; Grade 3 =severe or medically significant but not immediately life-threatening, hospitalization or prolongation of hospitalization indicated; Grade 4 =life-threatening or disabling, urgent intervention indicated; Grade 5 =death. Treatment-emergent events were events between first dose of study drug and up to 752 days that were absent before treatment that worsened relative to pretreatment state. If the same subject in a given treatment had more than 1 adverse event, only the maximum CTCAE was reported. Safety population included all subjects who received at least 1 dose of study medication with treatment assignments designated to actual study treatment received.	
End point type	Other pre-specified
End point timeframe: Baseline up to 752 days	

End point values	Bosutinib	Imatinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268	265		
Units: subjects				
Grade 1	20	44		
Grade 2	92	100		
Grade 3	120	90		

Grade 4	30	19		
Grade 5	1	4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 752 days

Adverse event reporting additional description:

Same event may appear as both an AE and serious adverse event. However, what is presented are distinct events. An event may be categorized as serious in one subject and as non-serious in another, or a subject may have experienced both a serious and non-serious event.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	Bosutinib
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Reporting group description:

Subjects with Philadelphia chromosome-positive CML received bosutinib at a dose of 400 mg, orally once daily in the core treatment period of 12 months. Subjects who completed the core treatment period, entered into extension period and received same treatment.

Reporting group title	Imatinib
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Reporting group description:

Subjects with Philadelphia chromosome-positive CML received imatinib at a dose of 400 mg, orally once daily in the core treatment period of 12 months. Subjects who completed the core treatment period, entered into extension period and received same treatment.

Serious adverse events	Bosutinib	Imatinib	
Total subjects affected by serious adverse events			
subjects affected / exposed	54 / 268 (20.15%)	45 / 265 (16.98%)	
number of deaths (all causes)	0	4	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
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	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			

subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic adenoma			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			

subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 268 (1.49%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthermia			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implant site haematoma			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatic dysplasia			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Uterine haemorrhage			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary toxicity			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory failure			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 268 (1.12%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood sodium decreased			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			

subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			

subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Headache			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 268 (0.37%)	3 / 265 (1.13%)	
occurrences causally related to treatment / all	1 / 1	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	2 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			

subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal vein occlusion			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 268 (1.12%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	3 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal necrosis			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diverticulum intestinal			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food poisoning			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatotoxicity			

subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis allergic			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lichen planus			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
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	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Swelling face			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Calculus bladder			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
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	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteochondrosis			
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Arthralgia			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	4 / 268 (1.49%)	3 / 265 (1.13%)	
occurrences causally related to treatment / all	0 / 4	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastroenteritis			
subjects affected / exposed	5 / 268 (1.87%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	4 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Subcutaneous abscess			
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			

subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida pneumonia			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective pericardial effusion			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis			

subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic infection			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic infection			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour lysis syndrome			

subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Bosutinib	Imatinib	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	263 / 268 (98.13%)	257 / 265 (96.98%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	3 / 268 (1.12%)	0 / 265 (0.00%)	
occurrences (all)	3	0	
Acanthoma			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Adrenal adenoma			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Prostatic adenoma			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Seborrhoeic keratosis			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Skin cancer			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Anogenital warts			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Leukaemic retinopathy			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Skin papilloma			

subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	1 / 265 (0.38%) 1	
Lipoma subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Melanocytic naevus subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Vascular disorders			
Hypertension subjects affected / exposed occurrences (all)	13 / 268 (4.85%) 13	16 / 265 (6.04%) 16	
Haematoma subjects affected / exposed occurrences (all)	5 / 268 (1.87%) 5	3 / 265 (1.13%) 3	
Hypotension subjects affected / exposed occurrences (all)	5 / 268 (1.87%) 5	5 / 265 (1.89%) 5	
Angiopathy subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Capillary fragility subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Deep vein thrombosis subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Flushing subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Hot flush subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	1 / 265 (0.38%) 1	
Jugular vein distension subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	

Orthostatic hypotension subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	1 / 265 (0.38%) 1	
Pallor subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	1 / 265 (0.38%) 1	
Periphlebitis subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Phlebitis subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	2 / 265 (0.75%) 2	
Venous thrombosis limb subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Iliac artery occlusion subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Peripheral coldness subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	2 / 265 (0.75%) 2	
Surgical and medical procedures			
Cholecystectomy subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Debridement subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Hernia hiatus repair subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Hip arthroplasty subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Inguinal hernia repair			

subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Medical induction of coma			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Tooth extraction			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Transfusion			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Cyst drainage			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Endodontic procedure			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Vitrectomy			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Muscle pain/ Joint pain			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	54 / 268 (20.15%)	47 / 265 (17.74%)	
occurrences (all)	54	47	
Pyrexia			
subjects affected / exposed	33 / 268 (12.31%)	21 / 265 (7.92%)	
occurrences (all)	33	21	
Asthenia			
subjects affected / exposed	32 / 268 (11.94%)	18 / 265 (6.79%)	
occurrences (all)	32	18	
Oedema peripheral			

subjects affected / exposed	12 / 268 (4.48%)	36 / 265 (13.58%)
occurrences (all)	12	36
Influenza like illness		
subjects affected / exposed	10 / 268 (3.73%)	3 / 265 (1.13%)
occurrences (all)	10	3
Non-cardiac chest pain		
subjects affected / exposed	9 / 268 (3.36%)	6 / 265 (2.26%)
occurrences (all)	9	6
Chills		
subjects affected / exposed	7 / 268 (2.61%)	6 / 265 (2.26%)
occurrences (all)	7	6
Chest pain		
subjects affected / exposed	5 / 268 (1.87%)	6 / 265 (2.26%)
occurrences (all)	5	6
Face oedema		
subjects affected / exposed	5 / 268 (1.87%)	15 / 265 (5.66%)
occurrences (all)	5	15
Pain		
subjects affected / exposed	4 / 268 (1.49%)	8 / 265 (3.02%)
occurrences (all)	4	8
Feeling hot		
subjects affected / exposed	3 / 268 (1.12%)	0 / 265 (0.00%)
occurrences (all)	3	0
Malaise		
subjects affected / exposed	3 / 268 (1.12%)	4 / 265 (1.51%)
occurrences (all)	3	4
Peripheral swelling		
subjects affected / exposed	3 / 268 (1.12%)	4 / 265 (1.51%)
occurrences (all)	3	4
Chest discomfort		
subjects affected / exposed	2 / 268 (0.75%)	3 / 265 (1.13%)
occurrences (all)	2	3
Mucosal inflammation		
subjects affected / exposed	2 / 268 (0.75%)	1 / 265 (0.38%)
occurrences (all)	2	1
Cyst		

subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)
occurrences (all)	1	2
Discomfort		
subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)
occurrences (all)	1	2
Early satiety		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Granuloma		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Mucosal dryness		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Thirst		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Xerosis		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Axillary pain		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Feeling abnormal		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Feeling cold		
subjects affected / exposed	0 / 268 (0.00%)	6 / 265 (2.26%)
occurrences (all)	0	6
Impaired healing		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Local swelling		
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)
occurrences (all)	0	2
Nodule		

subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Polyp subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Swelling subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Ulcer subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	2 / 268 (0.75%) 2	2 / 265 (0.75%) 2	
Food allergy subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Rubber sensitivity subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Seasonal allergy subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	2 / 265 (0.75%) 2	
Drug hypersensitivity subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	2 / 265 (0.75%) 2	
Reproductive system and breast disorders Amenorrhoea subjects affected / exposed occurrences (all)	2 / 268 (0.75%) 2	2 / 265 (0.75%) 2	
Benign prostatic hyperplasia subjects affected / exposed occurrences (all)	2 / 268 (0.75%) 2	2 / 265 (0.75%) 2	
Dysmenorrhoea			

subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)
occurrences (all)	2	0
Menstruation irregular		
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)
occurrences (all)	2	0
Adnexa uteri cyst		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Breast haematoma		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Endometriosis		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Menopausal symptoms		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Menorrhagia		
subjects affected / exposed	1 / 268 (0.37%)	3 / 265 (1.13%)
occurrences (all)	1	3
Prostatitis		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Prostatomegaly		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Testicular mass		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Erectile dysfunction		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Genital haemorrhage		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Menstruation delayed		

subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Pelvic pain			
subjects affected / exposed	0 / 268 (0.00%)	4 / 265 (1.51%)	
occurrences (all)	0	4	
Prostatic dysplasia			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Sexual dysfunction			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Vaginal haemorrhage			
subjects affected / exposed	0 / 268 (0.00%)	3 / 265 (1.13%)	
occurrences (all)	0	3	
Vulvovaginal pruritus			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	22 / 268 (8.21%)	10 / 265 (3.77%)	
occurrences (all)	22	10	
Cough			
subjects affected / exposed	21 / 268 (7.84%)	18 / 265 (6.79%)	
occurrences (all)	21	18	
Oropharyngeal pain			
subjects affected / exposed	13 / 268 (4.85%)	9 / 265 (3.40%)	
occurrences (all)	13	9	
Epistaxis			
subjects affected / exposed	10 / 268 (3.73%)	7 / 265 (2.64%)	
occurrences (all)	10	7	
Pleural effusion			
subjects affected / exposed	4 / 268 (1.49%)	3 / 265 (1.13%)	
occurrences (all)	4	3	
Productive cough			

subjects affected / exposed	4 / 268 (1.49%)	3 / 265 (1.13%)
occurrences (all)	4	3
Rhinorrhoea		
subjects affected / exposed	3 / 268 (1.12%)	2 / 265 (0.75%)
occurrences (all)	3	2
Asthma		
subjects affected / exposed	2 / 268 (0.75%)	1 / 265 (0.38%)
occurrences (all)	2	1
Catarrh		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Chronic obstructive pulmonary disease		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Dysphonia		
subjects affected / exposed	1 / 268 (0.37%)	4 / 265 (1.51%)
occurrences (all)	1	4
Emphysema		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Haemoptysis		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Lung infiltration		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Nasal congestion		
subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)
occurrences (all)	1	2
Pleuritic pain		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Respiratory tract congestion		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0

Rhinitis allergic		
subjects affected / exposed	1 / 268 (0.37%)	3 / 265 (1.13%)
occurrences (all)	1	3
Sinus congestion		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Throat irritation		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Throat tightness		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Tonsillar hypertrophy		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Wheezing		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Dry throat		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Dyspnoea exertional		
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)
occurrences (all)	0	2
Hypoxia		
subjects affected / exposed	0 / 268 (0.00%)	3 / 265 (1.13%)
occurrences (all)	0	3
Laryngeal inflammation		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Nasal ulcer		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Rales		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1

Respiratory failure subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Sneezing subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Upper-airway cough syndrome subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	15 / 268 (5.60%) 15	16 / 265 (6.04%) 16	
Anxiety subjects affected / exposed occurrences (all)	10 / 268 (3.73%) 10	10 / 265 (3.77%) 10	
Depression subjects affected / exposed occurrences (all)	8 / 268 (2.99%) 8	10 / 265 (3.77%) 10	
Libido decreased subjects affected / exposed occurrences (all)	2 / 268 (0.75%) 2	0 / 265 (0.00%) 0	
Confusional state subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	1 / 265 (0.38%) 1	
Delirium subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Depressive symptom subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Mood altered subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Sleep disorder			

subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	1 / 265 (0.38%) 1	
Irritability subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Mood swings subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	2 / 265 (0.75%) 2	
Nightmare subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	81 / 268 (30.22%) 81	15 / 265 (5.66%) 15	
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	60 / 268 (22.39%) 60	17 / 265 (6.42%) 17	
Lipase increased subjects affected / exposed occurrences (all)	36 / 268 (13.43%) 36	22 / 265 (8.30%) 22	
Platelet count decreased subjects affected / exposed occurrences (all)	33 / 268 (12.31%) 33	20 / 265 (7.55%) 20	
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	15 / 268 (5.60%) 15	9 / 265 (3.40%) 9	
Blood creatinine increased subjects affected / exposed occurrences (all)	15 / 268 (5.60%) 15	17 / 265 (6.42%) 17	
Amylase increased subjects affected / exposed occurrences (all)	14 / 268 (5.22%) 14	7 / 265 (2.64%) 7	
Blood bilirubin increased			

subjects affected / exposed	13 / 268 (4.85%)	6 / 265 (2.26%)
occurrences (all)	13	6
Blood creatine phosphokinase increased		
subjects affected / exposed	9 / 268 (3.36%)	19 / 265 (7.17%)
occurrences (all)	9	19
Weight decreased		
subjects affected / exposed	8 / 268 (2.99%)	5 / 265 (1.89%)
occurrences (all)	8	5
Weight increased		
subjects affected / exposed	8 / 268 (2.99%)	13 / 265 (4.91%)
occurrences (all)	8	13
Blood uric acid increased		
subjects affected / exposed	7 / 268 (2.61%)	2 / 265 (0.75%)
occurrences (all)	7	2
Transaminases increased		
subjects affected / exposed	7 / 268 (2.61%)	2 / 265 (0.75%)
occurrences (all)	7	2
Blood cholesterol increased		
subjects affected / exposed	6 / 268 (2.24%)	1 / 265 (0.38%)
occurrences (all)	6	1
Gamma-glutamyltransferase increased		
subjects affected / exposed	6 / 268 (2.24%)	4 / 265 (1.51%)
occurrences (all)	6	4
White blood cell count decreased		
subjects affected / exposed	6 / 268 (2.24%)	14 / 265 (5.28%)
occurrences (all)	6	14
Electrocardiogram QT prolonged		
subjects affected / exposed	4 / 268 (1.49%)	8 / 265 (3.02%)
occurrences (all)	4	8
Hepatic enzyme increased		
subjects affected / exposed	4 / 268 (1.49%)	0 / 265 (0.00%)
occurrences (all)	4	0
Neutrophil count decreased		

subjects affected / exposed	4 / 268 (1.49%)	11 / 265 (4.15%)
occurrences (all)	4	11
Blood urea increased		
subjects affected / exposed	3 / 268 (1.12%)	2 / 265 (0.75%)
occurrences (all)	3	2
Haemoglobin decreased		
subjects affected / exposed	3 / 268 (1.12%)	4 / 265 (1.51%)
occurrences (all)	3	4
Lymphocyte count decreased		
subjects affected / exposed	3 / 268 (1.12%)	4 / 265 (1.51%)
occurrences (all)	3	4
Blood glucose increased		
subjects affected / exposed	2 / 268 (0.75%)	3 / 265 (1.13%)
occurrences (all)	2	3
Blood lactate dehydrogenase increased		
subjects affected / exposed	2 / 268 (0.75%)	1 / 265 (0.38%)
occurrences (all)	2	1
Liver function test increased		
subjects affected / exposed	2 / 268 (0.75%)	1 / 265 (0.38%)
occurrences (all)	2	1
White blood cell count increased		
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)
occurrences (all)	2	0
Activated partial thromboplastin time prolonged		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Aspartate aminotransferase		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Blood bicarbonate decreased		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Blood chloride increased		

subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Blood iron decreased		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Blood phosphorus decreased		
subjects affected / exposed	1 / 268 (0.37%)	3 / 265 (1.13%)
occurrences (all)	1	3
Blood urine present		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
C-reactive protein increased		
subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)
occurrences (all)	1	2
Cardiac murmur		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Electrocardiogram QT interval		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Electrocardiogram ST-T segment abnormal		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Electrocardiogram T wave amplitude decreased		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Eosinophil count decreased		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Occult blood positive		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Platelet count increased		

subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Protein urine		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Serum ferritin decreased		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Basophil count increased		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Blood creatine phosphokinase MB increased		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Blood folate decreased		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Blood magnesium decreased		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Blood potassium decreased		
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)
occurrences (all)	0	2
Blood pressure systolic increased		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Blood triglycerides increased		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Body temperature increased		
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)
occurrences (all)	0	2
Eosinophil count increased		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1

Globulins decreased		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Heart rate increased		
subjects affected / exposed	0 / 268 (0.00%)	4 / 265 (1.51%)
occurrences (all)	0	4
Heart rate irregular		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
International normalised ratio increased		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Lipids abnormal		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Lymph node palpable		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Lymphocyte count increased		
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)
occurrences (all)	0	2
Neutrophil count increased		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Nicotinamide decreased		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Prostatic specific antigen increased		
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)
occurrences (all)	0	2
Protein total decreased		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Prothrombin time prolonged		

subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Pulmonary arterial pressure increased			
subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Urinary sediment present			
subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Bilirubin conjugated increased			
subjects affected / exposed occurrences (all)	2 / 268 (0.75%) 2	0 / 265 (0.00%) 0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed occurrences (all)	7 / 268 (2.61%) 7	3 / 265 (1.13%) 3	
Fall			
subjects affected / exposed occurrences (all)	4 / 268 (1.49%) 4	0 / 265 (0.00%) 0	
Arthropod bite			
subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Hand fracture			
subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Heavy exposure to ultraviolet light			
subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Laceration			
subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	1 / 265 (0.38%) 1	
Ligament sprain			
subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1	0 / 265 (0.00%) 0	
Limb injury			

subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Lip injury		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Nerve injury		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Post procedural haematoma		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Procedural pain		
subjects affected / exposed	1 / 268 (0.37%)	3 / 265 (1.13%)
occurrences (all)	1	3
Radius fracture		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Rib fracture		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Spinal fracture		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Sunburn		
subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)
occurrences (all)	1	2
Tooth fracture		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Wound dehiscence		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Animal bite		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Eye injury		

subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Gun shot wound			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Keratorhexis			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Muscle rupture			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Muscle strain			
subjects affected / exposed	0 / 268 (0.00%)	3 / 265 (1.13%)	
occurrences (all)	0	3	
Poisoning			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Skin abrasion			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Wound			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Ankle fracture			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Foot fracture			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Congenital, familial and genetic disorders			
Trisomy 8			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Cytogenetic abnormality			

subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Cardiac disorders			
Palpitations			
subjects affected / exposed	5 / 268 (1.87%)	8 / 265 (3.02%)	
occurrences (all)	5	8	
Sinus bradycardia			
subjects affected / exposed	4 / 268 (1.49%)	0 / 265 (0.00%)	
occurrences (all)	4	0	
Atrial fibrillation			
subjects affected / exposed	3 / 268 (1.12%)	1 / 265 (0.38%)	
occurrences (all)	3	1	
Angina pectoris			
subjects affected / exposed	3 / 268 (1.12%)	1 / 265 (0.38%)	
occurrences (all)	3	1	
Bradycardia			
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)	
occurrences (all)	2	0	
Myocardial ischaemia			
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)	
occurrences (all)	2	0	
Diastolic dysfunction			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Extrasystoles			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Pericardial effusion			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Supraventricular extrasystoles			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)	
occurrences (all)	1	1	

Tachycardia			
subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)	
occurrences (all)	1	2	
Ventricular extrasystoles			
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)	
occurrences (all)	1	1	
Bundle branch block right			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Left ventricular hypertrophy			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Sinus tachycardia			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Tricuspid valve incompetence			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	49 / 268 (18.28%)	35 / 265 (13.21%)	
occurrences (all)	49	35	
Dizziness			
subjects affected / exposed	19 / 268 (7.09%)	19 / 265 (7.17%)	
occurrences (all)	19	19	
Paraesthesia			
subjects affected / exposed	6 / 268 (2.24%)	2 / 265 (0.75%)	
occurrences (all)	6	2	
Lethargy			
subjects affected / exposed	5 / 268 (1.87%)	6 / 265 (2.26%)	
occurrences (all)	5	6	
Memory impairment			
subjects affected / exposed	5 / 268 (1.87%)	2 / 265 (0.75%)	
occurrences (all)	5	2	
Disturbance in attention			

subjects affected / exposed	4 / 268 (1.49%)	1 / 265 (0.38%)
occurrences (all)	4	1
Dysgeusia		
subjects affected / exposed	4 / 268 (1.49%)	9 / 265 (3.40%)
occurrences (all)	4	9
Hypoaesthesia		
subjects affected / exposed	4 / 268 (1.49%)	2 / 265 (0.75%)
occurrences (all)	4	2
Peripheral sensory neuropathy		
subjects affected / exposed	4 / 268 (1.49%)	1 / 265 (0.38%)
occurrences (all)	4	1
Dysaesthesia		
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)
occurrences (all)	2	0
Amnesia		
subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)
occurrences (all)	1	2
Ataxia		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Burning sensation		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Dizziness postural		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Migraine		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Muscle contractions involuntary		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Nerve compression		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Neuralgia		

subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Neuropathy peripheral		
subjects affected / exposed	1 / 268 (0.37%)	3 / 265 (1.13%)
occurrences (all)	1	3
Peripheral motor neuropathy		
subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)
occurrences (all)	1	2
Presyncope		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Sciatica		
subjects affected / exposed	1 / 268 (0.37%)	4 / 265 (1.51%)
occurrences (all)	1	4
Somnolence		
subjects affected / exposed	1 / 268 (0.37%)	6 / 265 (2.26%)
occurrences (all)	1	6
Syncope		
subjects affected / exposed	1 / 268 (0.37%)	4 / 265 (1.51%)
occurrences (all)	1	4
Tremor		
subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)
occurrences (all)	1	2
Ageusia		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Balance disorder		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Intercostal neuralgia		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Migraine with aura		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Restless legs syndrome		

subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	63 / 268 (23.51%)	32 / 265 (12.08%)	
occurrences (all)	63	32	
Anaemia			
subjects affected / exposed	47 / 268 (17.54%)	52 / 265 (19.62%)	
occurrences (all)	47	52	
Neutropenia			
subjects affected / exposed	26 / 268 (9.70%)	44 / 265 (16.60%)	
occurrences (all)	26	44	
Leukopenia			
subjects affected / exposed	9 / 268 (3.36%)	15 / 265 (5.66%)	
occurrences (all)	9	15	
Lymphopenia			
subjects affected / exposed	8 / 268 (2.99%)	3 / 265 (1.13%)	
occurrences (all)	8	3	
Leukocytosis			
subjects affected / exposed	7 / 268 (2.61%)	4 / 265 (1.51%)	
occurrences (all)	7	4	
Increased tendency to bruise			
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)	
occurrences (all)	2	0	
Thrombocytosis			
subjects affected / exposed	2 / 268 (0.75%)	5 / 265 (1.89%)	
occurrences (all)	2	5	
Haemorrhagic anaemia			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)	
occurrences (all)	1	1	
Lymphadenopathy			
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)	
occurrences (all)	1	1	

Lymphocytosis			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Mastocytosis			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Microcytosis			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Normochromic normocytic anaemia			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Pancytopenia			
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)	
occurrences (all)	1	1	
Eosinophilia			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Granulocytopenia			
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)	
occurrences (all)	0	2	
Monocytopenia			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Spontaneous haematoma			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	5 / 268 (1.87%)	2 / 265 (0.75%)	
occurrences (all)	5	2	
Tinnitus			
subjects affected / exposed	5 / 268 (1.87%)	1 / 265 (0.38%)	
occurrences (all)	5	1	
Vertigo			

subjects affected / exposed	3 / 268 (1.12%)	5 / 265 (1.89%)	
occurrences (all)	3	5	
Cerumen impaction			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Deafness			
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)	
occurrences (all)	1	1	
Inner ear inflammation			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Vertigo positional			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Hypoacusis			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Eye disorders			
Eye swelling			
subjects affected / exposed	4 / 268 (1.49%)	10 / 265 (3.77%)	
occurrences (all)	4	10	
Periorbital oedema			
subjects affected / exposed	4 / 268 (1.49%)	37 / 265 (13.96%)	
occurrences (all)	4	37	
Vision blurred			
subjects affected / exposed	4 / 268 (1.49%)	12 / 265 (4.53%)	
occurrences (all)	4	12	
Eye pain			
subjects affected / exposed	3 / 268 (1.12%)	7 / 265 (2.64%)	
occurrences (all)	3	7	
Conjunctival haemorrhage			
subjects affected / exposed	2 / 268 (0.75%)	8 / 265 (3.02%)	
occurrences (all)	2	8	
Eye haemorrhage			
subjects affected / exposed	2 / 268 (0.75%)	2 / 265 (0.75%)	
occurrences (all)	2	2	

Eye pruritus		
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)
occurrences (all)	2	0
Ocular hyperaemia		
subjects affected / exposed	2 / 268 (0.75%)	3 / 265 (1.13%)
occurrences (all)	2	3
Photophobia		
subjects affected / exposed	2 / 268 (0.75%)	1 / 265 (0.38%)
occurrences (all)	2	1
Retinal haemorrhage		
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)
occurrences (all)	2	0
Vitreous floaters		
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)
occurrences (all)	2	0
Cataract		
subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)
occurrences (all)	1	2
Conjunctivitis allergic		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Eye irritation		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Eyelid oedema		
subjects affected / exposed	1 / 268 (0.37%)	25 / 265 (9.43%)
occurrences (all)	1	25
Eyelid ptosis		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Lacrimal disorder		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Ocular discomfort		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0

Retinal disorder		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Uveitis		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Visual acuity reduced		
subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)
occurrences (all)	1	2
Visual impairment		
subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)
occurrences (all)	1	2
Vitreous detachment		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Conjunctival hyperaemia		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Diabetic retinopathy		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Diplopia		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Dry eye		
subjects affected / exposed	0 / 268 (0.00%)	11 / 265 (4.15%)
occurrences (all)	0	11
Eye discharge		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Eye oedema		
subjects affected / exposed	0 / 268 (0.00%)	4 / 265 (1.51%)
occurrences (all)	0	4
Eyelid pain		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1

Glaucoma			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Hypermetropia			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Lacrimation increased			
subjects affected / exposed	0 / 268 (0.00%)	16 / 265 (6.04%)	
occurrences (all)	0	16	
Ocular toxicity			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Orbital oedema			
subjects affected / exposed	0 / 268 (0.00%)	6 / 265 (2.26%)	
occurrences (all)	0	6	
Retinal detachment			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Retinopathy haemorrhagic			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Scleral haemorrhage			
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	189 / 268 (70.52%)	88 / 265 (33.21%)	
occurrences (all)	189	88	
Nausea			
subjects affected / exposed	94 / 268 (35.07%)	102 / 265 (38.49%)	
occurrences (all)	94	102	
Vomiting			
subjects affected / exposed	48 / 268 (17.91%)	43 / 265 (16.23%)	
occurrences (all)	48	43	
Abdominal pain			

subjects affected / exposed	47 / 268 (17.54%)	19 / 265 (7.17%)
occurrences (all)	47	19
Constipation		
subjects affected / exposed	26 / 268 (9.70%)	14 / 265 (5.28%)
occurrences (all)	26	14
Abdominal pain upper		
subjects affected / exposed	20 / 268 (7.46%)	19 / 265 (7.17%)
occurrences (all)	20	19
Dyspepsia		
subjects affected / exposed	18 / 268 (6.72%)	19 / 265 (7.17%)
occurrences (all)	18	19
Haemorrhoids		
subjects affected / exposed	10 / 268 (3.73%)	4 / 265 (1.51%)
occurrences (all)	10	4
Abdominal distension		
subjects affected / exposed	8 / 268 (2.99%)	3 / 265 (1.13%)
occurrences (all)	8	3
Toothache		
subjects affected / exposed	6 / 268 (2.24%)	3 / 265 (1.13%)
occurrences (all)	6	3
Flatulence		
subjects affected / exposed	5 / 268 (1.87%)	4 / 265 (1.51%)
occurrences (all)	5	4
Gastrooesophageal reflux disease		
subjects affected / exposed	5 / 268 (1.87%)	8 / 265 (3.02%)
occurrences (all)	5	8
Abdominal discomfort		
subjects affected / exposed	4 / 268 (1.49%)	6 / 265 (2.26%)
occurrences (all)	4	6
Dry mouth		
subjects affected / exposed	4 / 268 (1.49%)	7 / 265 (2.64%)
occurrences (all)	4	7
Mouth ulceration		
subjects affected / exposed	4 / 268 (1.49%)	3 / 265 (1.13%)
occurrences (all)	4	3
Haematochezia		

subjects affected / exposed	3 / 268 (1.12%)	0 / 265 (0.00%)
occurrences (all)	3	0
Epigastric discomfort		
subjects affected / exposed	2 / 268 (0.75%)	2 / 265 (0.75%)
occurrences (all)	2	2
Gastritis		
subjects affected / exposed	2 / 268 (0.75%)	2 / 265 (0.75%)
occurrences (all)	2	2
Paraesthesia oral		
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)
occurrences (all)	2	0
Proctalgia		
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)
occurrences (all)	2	0
Rectal haemorrhage		
subjects affected / exposed	2 / 268 (0.75%)	3 / 265 (1.13%)
occurrences (all)	2	3
Abdominal hernia		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Anal fissure		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Anal incontinence		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Aphthous ulcer		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Colitis		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Colitis ulcerative		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Dental caries		

subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Dental discomfort		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Dysphagia		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Faeces discoloured		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Food poisoning		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Gastric disorder		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Gastric ulcer		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Gastrointestinal disorder		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Gastrointestinal necrosis		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Gastrointestinal pain		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Duodenitis		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Glossodynia		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Gingival erythema		

subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Ileus		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Lip pain		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Oral pain		
subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)
occurrences (all)	1	2
Mouth haemorrhage		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Pancreatitis		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Peristalsis visible		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Proctitis		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Rectal tenesmus		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Retching		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Salivary gland enlargement		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Stomatitis		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Tongue discolouration		

subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Tongue disorder		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Abdominal pain lower		
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)
occurrences (all)	0	2
Anal haemorrhage		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Ascites		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Chronic gastritis		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Eructation		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Faeces soft		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Frequent bowel movements		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Gingival bleeding		
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)
occurrences (all)	0	2
Gingival pain		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Haematemesis		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Inguinal hernia		

subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)	
occurrences (all)	0	2	
Large intestine polyp			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Lip dry			
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)	
occurrences (all)	0	2	
Lip swelling			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Oesophagitis			
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)	
occurrences (all)	0	2	
Salivary hypersecretion			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Tongue dry			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Tooth disorder			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Umbilical hernia			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	4 / 268 (1.49%)	0 / 265 (0.00%)	
occurrences (all)	4	0	
Hyperbilirubinaemia			
subjects affected / exposed	4 / 268 (1.49%)	1 / 265 (0.38%)	
occurrences (all)	4	1	
Drug-induced liver injury			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	

Hepatitis			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Hepatitis toxic			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Hepatocellular injury			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Jaundice			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Cholestasis			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Hepatic steatosis			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Liver disorder			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	53 / 268 (19.78%)	36 / 265 (13.58%)	
occurrences (all)	53	36	
Pruritus			
subjects affected / exposed	25 / 268 (9.33%)	7 / 265 (2.64%)	
occurrences (all)	25	7	
Rash maculo-papular			
subjects affected / exposed	14 / 268 (5.22%)	14 / 265 (5.28%)	
occurrences (all)	14	14	
Alopecia			
subjects affected / exposed	12 / 268 (4.48%)	12 / 265 (4.53%)	
occurrences (all)	12	12	
Dry skin			

subjects affected / exposed	12 / 268 (4.48%)	10 / 265 (3.77%)
occurrences (all)	12	10
Erythema		
subjects affected / exposed	9 / 268 (3.36%)	4 / 265 (1.51%)
occurrences (all)	9	4
Rash pruritic		
subjects affected / exposed	7 / 268 (2.61%)	0 / 265 (0.00%)
occurrences (all)	7	0
Acne		
subjects affected / exposed	6 / 268 (2.24%)	1 / 265 (0.38%)
occurrences (all)	6	1
Dermatitis acneiform		
subjects affected / exposed	5 / 268 (1.87%)	1 / 265 (0.38%)
occurrences (all)	5	1
Urticaria		
subjects affected / exposed	5 / 268 (1.87%)	3 / 265 (1.13%)
occurrences (all)	5	3
Eczema		
subjects affected / exposed	4 / 268 (1.49%)	6 / 265 (2.26%)
occurrences (all)	4	6
Hyperhidrosis		
subjects affected / exposed	4 / 268 (1.49%)	6 / 265 (2.26%)
occurrences (all)	4	6
Rash papular		
subjects affected / exposed	4 / 268 (1.49%)	0 / 265 (0.00%)
occurrences (all)	4	0
Dermatitis		
subjects affected / exposed	3 / 268 (1.12%)	1 / 265 (0.38%)
occurrences (all)	3	1
Nail discolouration		
subjects affected / exposed	3 / 268 (1.12%)	1 / 265 (0.38%)
occurrences (all)	3	1
Rash erythematous		
subjects affected / exposed	3 / 268 (1.12%)	2 / 265 (0.75%)
occurrences (all)	3	2
Skin lesion		

subjects affected / exposed	3 / 268 (1.12%)	1 / 265 (0.38%)
occurrences (all)	3	1
Actinic keratosis		
subjects affected / exposed	2 / 268 (0.75%)	1 / 265 (0.38%)
occurrences (all)	2	1
Dermatitis allergic		
subjects affected / exposed	2 / 268 (0.75%)	4 / 265 (1.51%)
occurrences (all)	2	4
Dyshidrotic eczema		
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)
occurrences (all)	2	0
Miliaria		
subjects affected / exposed	2 / 268 (0.75%)	1 / 265 (0.38%)
occurrences (all)	2	1
Pruritus generalised		
subjects affected / exposed	2 / 268 (0.75%)	1 / 265 (0.38%)
occurrences (all)	2	1
Skin discolouration		
subjects affected / exposed	2 / 268 (0.75%)	1 / 265 (0.38%)
occurrences (all)	2	1
Skin exfoliation		
subjects affected / exposed	2 / 268 (0.75%)	1 / 265 (0.38%)
occurrences (all)	2	1
Angioedema		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Blister		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Dermal cyst		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Dermatitis exfoliative		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Drug reaction with eosinophilia and		

systemic symptoms		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Ecchymosis		
subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)
occurrences (all)	1	2
Generalised erythema		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Hyperkeratosis		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Hypertrichosis		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Ingrowing nail		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Mucocutaneous ulceration		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Nail disorder		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Nail dystrophy		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Perivascular dermatitis		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Photosensitivity reaction		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Purpura		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0

Rash generalised		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Sebacous glands overactivity		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Skin fragility		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Skin mass		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Skin ulcer		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Swelling face		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Vitiligo		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Dandruff		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Diffuse alopecia		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Eczema asteatotic		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Erythema multiforme		
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)
occurrences (all)	0	2
Erythema nodosum		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1

Petechiae			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Psoriasis			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Rash macular			
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)	
occurrences (all)	0	2	
Skin hypopigmentation			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Stasis dermatitis			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Toxic skin eruption			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Papule			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Night sweats			
subjects affected / exposed	5 / 268 (1.87%)	9 / 265 (3.40%)	
occurrences (all)	5	9	
Renal and urinary disorders			
Nocturia			
subjects affected / exposed	3 / 268 (1.12%)	1 / 265 (0.38%)	
occurrences (all)	3	1	
Acute kidney injury			
subjects affected / exposed	2 / 268 (0.75%)	1 / 265 (0.38%)	
occurrences (all)	2	1	
Dysuria			
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)	
occurrences (all)	2	0	
Haematuria			

subjects affected / exposed	2 / 268 (0.75%)	6 / 265 (2.26%)
occurrences (all)	2	6
Pollakiuria		
subjects affected / exposed	2 / 268 (0.75%)	3 / 265 (1.13%)
occurrences (all)	2	3
Renal impairment		
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)
occurrences (all)	2	0
Urethritis noninfective		
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)
occurrences (all)	2	0
Bladder diverticulum		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Calculus urinary		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Chromaturia		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Nephritis		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Nephrocalcinosis		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Nephroptosis		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Oliguria		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Polyuria		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Proteinuria		

subjects affected / exposed	1 / 268 (0.37%)	3 / 265 (1.13%)	
occurrences (all)	1	3	
Renal cyst			
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)	
occurrences (all)	1	1	
Urinary tract pain			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Urine abnormality			
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)	
occurrences (all)	1	1	
Acute prerenal failure			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Calculus urethral			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Nephropathy			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Nephrotic syndrome			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Renal injury			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Urinary retention			
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)	
occurrences (all)	0	2	
Urinary tract inflammation			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)	
occurrences (all)	2	0	

Hyperparathyroidism			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Thyroid disorder			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Thyroid mass			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	32 / 268 (11.94%)	35 / 265 (13.21%)	
occurrences (all)	32	35	
Back pain			
subjects affected / exposed	22 / 268 (8.21%)	19 / 265 (7.17%)	
occurrences (all)	22	19	
Pain in extremity			
subjects affected / exposed	12 / 268 (4.48%)	34 / 265 (12.83%)	
occurrences (all)	12	34	
Myalgia			
subjects affected / exposed	8 / 268 (2.99%)	41 / 265 (15.47%)	
occurrences (all)	8	41	
Bone pain			
subjects affected / exposed	7 / 268 (2.61%)	18 / 265 (6.79%)	
occurrences (all)	7	18	
Musculoskeletal pain			
subjects affected / exposed	7 / 268 (2.61%)	8 / 265 (3.02%)	
occurrences (all)	7	8	
Muscle spasms			
subjects affected / exposed	6 / 268 (2.24%)	70 / 265 (26.42%)	
occurrences (all)	6	70	
Neck pain			
subjects affected / exposed	6 / 268 (2.24%)	4 / 265 (1.51%)	
occurrences (all)	6	4	
Musculoskeletal chest pain			

subjects affected / exposed	4 / 268 (1.49%)	0 / 265 (0.00%)
occurrences (all)	4	0
Flank pain		
subjects affected / exposed	3 / 268 (1.12%)	2 / 265 (0.75%)
occurrences (all)	3	2
Muscular weakness		
subjects affected / exposed	2 / 268 (0.75%)	1 / 265 (0.38%)
occurrences (all)	2	1
Osteoarthritis		
subjects affected / exposed	2 / 268 (0.75%)	3 / 265 (1.13%)
occurrences (all)	2	3
Spinal pain		
subjects affected / exposed	2 / 268 (0.75%)	1 / 265 (0.38%)
occurrences (all)	2	1
Synovial cyst		
subjects affected / exposed	2 / 268 (0.75%)	1 / 265 (0.38%)
occurrences (all)	2	1
Intervertebral disc disorder		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Joint effusion		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Joint instability		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Limb discomfort		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Muscle fatigue		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Musculoskeletal discomfort		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Myopathy		

subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Osteoporosis		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Rheumatoid arthritis		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Spinal column stenosis		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Spinal osteoarthritis		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Arthritis		
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)
occurrences (all)	0	2
Dupuytren's contracture		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Foot deformity		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Growing pains		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Intervertebral disc protrusion		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Joint laxity		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Joint stiffness		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Muscle contracture		

subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Muscle twitching			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)	
occurrences (all)	0	2	
Osteochondrosis			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Pain in jaw			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Rhabdomyolysis			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Tenosynovitis			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Torticollis			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Trismus			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Tendonitis			
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	26 / 268 (9.70%)	24 / 265 (9.06%)	
occurrences (all)	26	24	

Upper respiratory tract infection subjects affected / exposed occurrences (all)	23 / 268 (8.58%) 23	27 / 265 (10.19%) 27
Urinary tract infection subjects affected / exposed occurrences (all)	17 / 268 (6.34%) 17	9 / 265 (3.40%) 9
Bronchitis subjects affected / exposed occurrences (all)	8 / 268 (2.99%) 8	4 / 265 (1.51%) 4
Influenza subjects affected / exposed occurrences (all)	7 / 268 (2.61%) 7	8 / 265 (3.02%) 8
Sinusitis subjects affected / exposed occurrences (all)	7 / 268 (2.61%) 7	5 / 265 (1.89%) 5
Gastroenteritis subjects affected / exposed occurrences (all)	6 / 268 (2.24%) 6	5 / 265 (1.89%) 5
Folliculitis subjects affected / exposed occurrences (all)	5 / 268 (1.87%) 5	2 / 265 (0.75%) 2
Pharyngitis subjects affected / exposed occurrences (all)	5 / 268 (1.87%) 5	6 / 265 (2.26%) 6
Lower respiratory tract infection subjects affected / exposed occurrences (all)	4 / 268 (1.49%) 4	1 / 265 (0.38%) 1
Respiratory tract infection subjects affected / exposed occurrences (all)	4 / 268 (1.49%) 4	2 / 265 (0.75%) 2
Cellulitis subjects affected / exposed occurrences (all)	3 / 268 (1.12%) 3	0 / 265 (0.00%) 0
Conjunctivitis subjects affected / exposed occurrences (all)	3 / 268 (1.12%) 3	6 / 265 (2.26%) 6

Otitis media		
subjects affected / exposed	3 / 268 (1.12%)	2 / 265 (0.75%)
occurrences (all)	3	2
Pneumonia		
subjects affected / exposed	3 / 268 (1.12%)	1 / 265 (0.38%)
occurrences (all)	3	1
Rhinitis		
subjects affected / exposed	3 / 268 (1.12%)	5 / 265 (1.89%)
occurrences (all)	3	5
Viral infection		
subjects affected / exposed	3 / 268 (1.12%)	7 / 265 (2.64%)
occurrences (all)	3	7
Cystitis		
subjects affected / exposed	2 / 268 (0.75%)	1 / 265 (0.38%)
occurrences (all)	2	1
Ear infection		
subjects affected / exposed	2 / 268 (0.75%)	1 / 265 (0.38%)
occurrences (all)	2	1
Eye infection		
subjects affected / exposed	2 / 268 (0.75%)	2 / 265 (0.75%)
occurrences (all)	2	2
Gastroenteritis viral		
subjects affected / exposed	2 / 268 (0.75%)	2 / 265 (0.75%)
occurrences (all)	2	2
Oral herpes		
subjects affected / exposed	2 / 268 (0.75%)	2 / 265 (0.75%)
occurrences (all)	2	2
Candida infection		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Chlamydial infection		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Ear lobe infection		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0

Erysipelas		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Gastrointestinal infection		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Hepatitis B		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Herpes zoster		
subjects affected / exposed	1 / 268 (0.37%)	3 / 265 (1.13%)
occurrences (all)	1	3
Infection		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Lice infestation		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Lip infection		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Lymphadenitis bacterial		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Oral candidiasis		
subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)
occurrences (all)	1	2
Paronychia		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Pulpitis dental		
subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)
occurrences (all)	1	2
Respiratory tract infection viral		
subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)
occurrences (all)	1	2

Skin infection		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Staphylococcal infection		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Tooth abscess		
subjects affected / exposed	1 / 268 (0.37%)	2 / 265 (0.75%)
occurrences (all)	1	2
Tooth infection		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Adenovirus infection		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Carbuncle		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Diarrhoea infectious		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Enterocolitis infectious		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Escherichia urinary tract infection		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Fungal skin infection		
subjects affected / exposed	0 / 268 (0.00%)	3 / 265 (1.13%)
occurrences (all)	0	3
Genital abscess		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Gingivitis		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1

Helicobacter infection		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Herpes simplex		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Hordeolum		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Labyrinthitis		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Localised infection		
subjects affected / exposed	0 / 268 (0.00%)	4 / 265 (1.51%)
occurrences (all)	0	4
Lung infection		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Meningococcal infection		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Nail infection		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Onychomycosis		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Parainfluenzae virus infection		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1
Pharyngitis streptococcal		
subjects affected / exposed	0 / 268 (0.00%)	2 / 265 (0.75%)
occurrences (all)	0	2
Pneumonia bacterial		
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)
occurrences (all)	0	1

Pyelonephritis chronic subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Tonsillitis bacterial subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Vaginal infection subjects affected / exposed occurrences (all)	0 / 268 (0.00%) 0	1 / 265 (0.38%) 1	
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	26 / 268 (9.70%) 26	16 / 265 (6.04%) 16	
Hyperuricaemia subjects affected / exposed occurrences (all)	5 / 268 (1.87%) 5	4 / 265 (1.51%) 4	
Hypophosphataemia subjects affected / exposed occurrences (all)	5 / 268 (1.87%) 5	14 / 265 (5.28%) 14	
Gout subjects affected / exposed occurrences (all)	4 / 268 (1.49%) 4	2 / 265 (0.75%) 2	
Hyperglycaemia subjects affected / exposed occurrences (all)	4 / 268 (1.49%) 4	8 / 265 (3.02%) 8	
Hyperkalaemia subjects affected / exposed occurrences (all)	4 / 268 (1.49%) 4	4 / 265 (1.51%) 4	
Hypertriglyceridaemia subjects affected / exposed occurrences (all)	4 / 268 (1.49%) 4	2 / 265 (0.75%) 2	
Hypokalaemia subjects affected / exposed occurrences (all)	4 / 268 (1.49%) 4	18 / 265 (6.79%) 18	
Hypercholesterolaemia			

subjects affected / exposed	3 / 268 (1.12%)	0 / 265 (0.00%)
occurrences (all)	3	0
Hypocalcaemia		
subjects affected / exposed	3 / 268 (1.12%)	8 / 265 (3.02%)
occurrences (all)	3	8
Hypomagnesaemia		
subjects affected / exposed	3 / 268 (1.12%)	2 / 265 (0.75%)
occurrences (all)	3	2
Vitamin D deficiency		
subjects affected / exposed	3 / 268 (1.12%)	0 / 265 (0.00%)
occurrences (all)	3	0
Dehydration		
subjects affected / exposed	2 / 268 (0.75%)	2 / 265 (0.75%)
occurrences (all)	2	2
Hyperchloraemia		
subjects affected / exposed	2 / 268 (0.75%)	0 / 265 (0.00%)
occurrences (all)	2	0
Hyponatraemia		
subjects affected / exposed	2 / 268 (0.75%)	2 / 265 (0.75%)
occurrences (all)	2	2
Diabetes mellitus		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Folate deficiency		
subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)
occurrences (all)	1	0
Hypoalbuminaemia		
subjects affected / exposed	1 / 268 (0.37%)	4 / 265 (1.51%)
occurrences (all)	1	4
Hypoglycaemia		
subjects affected / exposed	1 / 268 (0.37%)	5 / 265 (1.89%)
occurrences (all)	1	5
Iron deficiency		
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)
occurrences (all)	1	1
Obesity		

subjects affected / exposed	1 / 268 (0.37%)	0 / 265 (0.00%)	
occurrences (all)	1	0	
Vitamin B12 deficiency			
subjects affected / exposed	1 / 268 (0.37%)	1 / 265 (0.38%)	
occurrences (all)	1	1	
Electrolyte imbalance			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Fluid retention			
subjects affected / exposed	0 / 268 (0.00%)	8 / 265 (3.02%)	
occurrences (all)	0	8	
Hypermagnesaemia			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Increased appetite			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	
Metabolic syndrome			
subjects affected / exposed	0 / 268 (0.00%)	1 / 265 (0.38%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 March 2014	Updated information for assessments of vital signs, inclusion/exclusion criteria, laboratory assessments, timing of efficacy endpoints, exploratory efficacy endpoints, study durations, timing of assessments, terms and definitions, study populations, adverse event assessments, and administrative information.
14 January 2015	Updated information for contact details, study duration, subject populations, inclusion/exclusion criteria definitions, bosutinib formulation details, assessment timings (eg, schedule of events, pre-randomization Sokal score assessment), timing of assessments, timing for collection of adverse events/reporting, study drug dosing requirements, compliance recording, statistical analysis (primary and secondary efficacy analysis), pharmacokinetic analysis, and administrative information.
09 September 2016	Updated information for sample size, study populations, efficacy analysis, interim analyses, time to response description, and administrative information.
07 December 2016	Updated information for change of Sponsor details, sample size, study populations, methodology for statistical analyses, efficacy analysis, interim analyses, time to response description, extension phase visit window, sample drug diary cards, and administrative information.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported