Clinical trial results:
A Phase 3, Double-Blind, Placebo-Controlled Study of Maintenance Pemetrexed plus Best Supportive Care versus Best Supportive Care Immediately Following Induction Treatment for Advanced Non-Small Cell Lung Cancer

Summary

EudraCT number	2004-002425-52
Trial protocol	DE CZ AT HU IT ES
Global end of trial date	03 December 2013

Results information

Result version number	v1 (current)
This version publication date	04 July 2016
First version publication date	02 August 2015

Trial information

Trial identification

Sponsor protocol code	H3E-MC-JMEN

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00102804
WHO universal trial number (UTN)	-
Other trial identifiers	Trial ID Number: 5122

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon - Fri 9 AM - 5 PM EST , Eli Lilly and Company, 1 877-CTLilly,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST , Eli Lilly and Company, 1 877-285-4559,

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 December 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study is a randomized Phase 3, double-blind study of maintenance pemetrexed plus best supportive care versus placebo plus best supportive care in Non-Small Cell Lung Cancer (NSCLC). Participants must have received 1 of 6 induction regimens for 4 cycles and did not have progressive disease prior to randomization (enrollment) into this trial.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 March 2005
Long term follow-up planned	Yes
Long term follow-up rationale	Ethical reason
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	United States: 32
Country: Number of subjects enrolled	Taiwan: 9
Country: Number of subjects enrolled	Greece: 27
Country: Number of subjects enrolled	Spain: 49
Country: Number of subjects enrolled	Turkey: 11
Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	Italy: 34
Country: Number of subjects enrolled	Czech Republic: 7
Country: Number of subjects enrolled	Poland: 36
Country: Number of subjects enrolled	Brazil: 34
Country: Number of subjects enrolled	Croatia: 13
Country: Number of subjects enrolled	Romania: 77
Country: Number of subjects enrolled	Australia: 27
Country: Number of subjects enrolled	Bulgaria: 19
Country: Number of subjects enrolled	Netherlands: 14
Country: Number of subjects enrolled	Germany: 56
Country: Number of subjects enrolled	China: 99

Country: Number of subjects enrolled	Korea, Republic of: 46
Country: Number of subjects enrolled	India: 55
Country: Number of subjects enrolled	Hungary: 14
Worldwide total number of subjects	663
EEA total number of subjects	350

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)	443
From 65 to 84 years	220
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants who signed the informed consent form (ICF) and completed the randomized process are presented in the participant flow by the treatment arm to which they were randomized. Participants who did not sign the ICF or complete the randomization process were removed from the database and excluded from all analyses.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Pemetrexed and BSC

Arm description:

Pemetrexed: 500 milligrams per square meter (mg/m^2), intravenous (IV) administration, every (q) 21 days, until disease progression.

Best Supportive Care (BSC): Treatment without a specific antineoplastic regimen, given with the intent to maximize quality of life, as judged by the treating physician.

Arm type	Experimental
Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	LY231514, Alimta
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

500 milligrams per square meter (mg/m^2), intravenous (IV) administration, every (q) 21 days, until disease progression

Arm title	Placebo and Best Supportive Care (BSC)

Arm description:

Placebo: IV administration, q 21 days, until disease progression.

BSC: Treatment without a specific antineoplastic regimen, given with the intent to maximize quality of life, as judged by the treating physician.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV administration, q 21 days

Number of subjects in period 1	Pemetrexed and BSC	Placebo and Best Supportive Care (BSC)
Started	441	222
Received at least 1 dose of study drug	434	222
Completed	0	0
Not completed	441	222
Adverse event, serious fatal	5	6
Consent withdrawn by subject	46	7
Physician decision	24	6
Adverse event, non-fatal	37	3
Progressive Disease (PD)	307	196
Enrollment Criteria Not Met	6	-
Sponsor Decision	1	-
Alive, Receiving Treatment	7	2
Lost to follow-up	4	1
Satisfactory Response	2	-
Protocol deviation	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Pemetrexed and BSC

Reporting group description:

Pemetrexed: 500 milligrams per square meter (mg/m^2), intravenous (IV) administration, every (q) 21 days, until disease progression.

Best Supportive Care (BSC): Treatment without a specific antineoplastic regimen, given with the intent to maximize quality of life, as judged by the treating physician.

Reporting group title	Placebo and Best Supportive Care (BSC)

Reporting group description:

Placebo: IV administration, q 21 days, until disease progression.

BSC: Treatment without a specific antineoplastic regimen, given with the intent to maximize quality of life, as judged by the treating physician.

Reporting group values	Pemetrexed and BSC	Placebo and Best Supportive Care (BSC)	Total
Number of subjects	441	222	
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age Continuous Units: years			
median	60.6	60.4	
inter-quartile range (Q1-Q3)	54.3 to 67.5	53.8 to 67	-
Gender, Male/Female Units: participants			
Female			0
Male			0
Race/Ethnicity, Customized Units: Subjects			
Aboriginal			0
African			0
Caucasian			0
East Asian			0
Hispanic			0
West Asian			0

Subject analysis sets	
Subject analysis set title	Pemetrexed and BSC
Subject analysis set type	Full analysis

Subject analysis set description:

Pemetrexed: 500 milligrams per square meter (mg/m^2), intravenous (IV) administration, every (q) 21 days, until disease progression.
Best Supportive Care (BSC): Treatment without a specific antineoplastic regimen, given with the intent to maximize quality of life, as judged by the treating physician.

Subject analysis set title	Placebo and BSC
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo: IV administration, q 21 days, until disease progression.
BSC: Treatment without a specific antineoplastic regimen, given with the intent to maximize quality of life, as judged by the treating physician.

Reporting group values	Pemetrexed and BSC	Placebo and BSC	
Number of subjects	441	222	
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age Continuous Units: years			
median			
inter-quartile range (Q1-Q3)			
Gender, Male/Female Units: participants			
Female	119	61	
Male	322	161	
Race/Ethnicity, Customized Units: Subjects			
Aboriginal	0	1	
African	6	0	
Caucasian	279	149	
East Asian	104	50	
Hispanic	13	6	
West Asian	39	16	

End points

End points reporting groups

Reporting group title	Pemetrexed and BSC

Reporting group description:

Pemetrexed: 500 milligrams per square meter (mg/m^2), intravenous (IV) administration, every (q) 21 days, until disease progression.

Best Supportive Care (BSC): Treatment without a specific antineoplastic regimen, given with the intent to maximize quality of life, as judged by the treating physician.

Reporting group title	Placebo and Best Supportive Care (BSC)

Reporting group description:

Placebo: IV administration, q 21 days, until disease progression.

BSC: Treatment without a specific antineoplastic regimen, given with the intent to maximize quality of life, as judged by the treating physician.

Subject analysis set title	Pemetrexed and BSC
Subject analysis set type	Full analysis

Subject analysis set description:

Pemetrexed: 500 milligrams per square meter (mg/m^2), intravenous (IV) administration, every (q) 21 days, until disease progression.
Best Supportive Care (BSC): Treatment without a specific antineoplastic regimen, given with the intent to maximize quality of life, as judged by the treating physician.

Subject analysis set title	Placebo and BSC
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo: IV administration, q 21 days, until disease progression.
BSC: Treatment without a specific antineoplastic regimen, given with the intent to maximize quality of life, as judged by the treating physician.

Primary: Progression-Free survival (PFS) time

End point title	Progression-Free survival (PFS) time

End point description:

PFS time was the elapsed time from the date of randomization to the first date of objective progression of disease or death from any cause. PFS was censored at the date of the participant's last tumor assessment for participants who were not known to have died or to have PD as of the data-inclusion cut-off date for analysis. PD, defined using Response Evaluation Criteria in Solid Tumors version 1.0 (RECIST v1.0), was at least a 20% increase in the sum of longest diameter (LD) of target lesions taking as references the smallest sum LD recorded since the treatment started or the appearance of 1 or more new lesions.

End point type	Primary

End point timeframe:

Randomization to measured PD or death from any cause (up to 41 months)

End point values	Pemetrexed and BSC	Placebo and Best Supportive Care (BSC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	441	222		
Units: months				
median (confidence interval 95%)	4.27 (4.07 to 4.73)	2.6 (1.68 to 2.83)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1 for Primary Endpoint (PFS)

Statistical analysis description:

The study applied a statistical gatekeeping and alpha-spending scheme such that the statistical power for assessment of Overall Survival at the time of survival maturity will be maintained.

Comparison groups	Pemetrexed and BSC v Placebo and Best Supportive Care (BSC)
Number of subjects included in analysis	663
Analysis specification	Pre-specified
Analysis type	superiority[1]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	0.61

Notes:

[1] - The primary analysis estimated the PFS HR using a Cox proportional hazards model (Cox 1972) with
assigned treatment as the only covariate. The same hypothesis used for the primary analysis of PFS was used to compare all time-to-event variables (OS, TtP, and TWS).

Secondary: Overall survival (OS) time

End point title	Overall survival (OS) time

End point description:

OS time was the elapsed time from the date of randomization to the date of death from any cause. OS was censored at the last date of contact for participants who were not known to have died as of the data-inclusion cut-off date for analysis.

End point type	Secondary

End point timeframe:

Randomization to date of death from any cause (up to 41 months)

End point values	Pemetrexed and BSC	Placebo and Best Supportive Care (BSC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	441	222		
Units: months				
median (confidence interval 95%)	13.37 (11.93 to 15.87)	10.58 (8.74 to 12.02)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to objective progressive disease (TPD)

End point title	Time to objective progressive disease (TPD)

End point description:

TPD was the elapsed time from the date of randomization to the first date of objective PD. TPD was censored at the date of the participant's last tumor assessment for participants who were not known to have PD as of the data-inclusion cut-off date for analysis or who died without objective PD. PD, defined using RECIST v1.0, was at least a 20% increase in the sum of LD of target lesions taking as reference the smallest sum LD recorded since the treatment started or the appearance of 1 or more new lesions.

End point type	Secondary

End point timeframe:

Randomization to measured PD (up to 41 months)

End point values	Pemetrexed and BSC	Placebo and Best Supportive Care (BSC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	441	222		
Units: months				
median (confidence interval 95%)	4.27 (4.11 to 4.73)	2.6 (1.68 to 2.83)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to worsening of symptoms (TWS)

End point title	Time to worsening of symptoms (TWS)

End point description:

TWS was the elapsed time from the date of randomization to the first date of worsening [defined as a 15-millimeter (mm) increase from baseline based on a 100-mm scale] of each symptom and summary item in the Lung Cancer Symptom Scale (LCSS). The participant-reported LCSS was a 9-item questionnaire. Six items were symptom-specific measures for lung cancer (loss of appetite, fatigue, cough, dyspnea, hemoptysis, and pain), and 3 summation items described total symptomatic distress, interference with activity level, and global quality of life. Participant (pt) responses to each item were measured using visual analogue scales (VAS) from 0 (for best outcome) to 100 (for worst outcome). TWS was censored at the date of the last LCSS assessment for pts who were not known to have LCSS worsening.
*Median (95% confidence interval) TWS for hemoptysis was not calculated due to the high level of censoring.

End point type	Secondary

End point timeframe:

Randomization to worsening of each LCSS item (up to 39 months)

End point values	Pemetrexed and BSC	Placebo and Best Supportive Care (BSC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	441	222		
Units: months				
median (confidence interval 95%)				
Loss of appetite	3.78 (2.86 to 4.44)	4.4 (2.96 to 15.61)		
Fatigue	3.06 (2.63 to 5.29)	3.09 (2.43 to 3.98)		
Cough	6.05 (4.21 to 7.82)	4.67 (3.06 to 15.61)		
Dyspnea	5.36 (4.21 to 10.87)	4.4 (2.83 to 15.61)		
Hemoptysis	9999 (999 to 99999)	9999 (999 to 9999)		
Pain	6.11 (4.57 to 9.56)	4.63 (3.32 to 5.98)		
Symptomatic distress	4.21 (3.58 to 5.55)	3.78 (2.99 to 18.53)		
Interference with activity level	6.51 (4.34 to 8.18)	3.98 (2.83 to 15.61)		
Global quality of life	5.75 (4.37 to 8.41)	3.71 (2.99 to 5.49)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Complete Response (CR) or Partial Response (PR) (Objective tumor response rate)

End point title	Percentage of Participants with a Complete Response (CR) or Partial Response (PR) (Objective tumor response rate)

End point description:

Response was defined using RECIST v1.0 criteria. CR was defined as the disappearance of all target lesions. PR was defined either A) at least a 30% decrease in the sum of the LD of target lesions taking as reference the baseline sum LDs or B) complete disappearance of target lesions, with persistence (but not worsening) of 1 or more nontarget lesions. In either case, no new lesions may have appeared. The percentage of participants with CR or PR=(Number of participants with CR or PR)/(Number of participants assessed)*100.

End point type	Secondary

End point timeframe:

Baseline to measured PD (up to 41 months)

End point values	Pemetrexed and BSC	Placebo and Best Supportive Care (BSC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	441	222		
Units: percentage of participants				
number (confidence interval 95%)	6.8 (5 to 10)	1.8 (0 to 5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events (AEs)

End point title	Number of Participants With Adverse Events (AEs)

End point description:

Clinically significant events were defined as serious adverse events (SAEs) and other non-serious AEs regardless of causality. A summary of serious and other non-serious AEs, regardless of causality, is located in the Reported Adverse Events module.

End point type	Secondary

End point timeframe:

Baseline to study completion (up to 41 Months)

End point values	Pemetrexed and BSC	Placebo and Best Supportive Care (BSC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	438	218		
Units: participants				
number (not applicable)				
SAEs	83	31		
Other Non-Serious AEs	386	178		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Improvement Over Baseline in individual symptom scores and quality of life using the LCSS

End point title	Maximum Improvement Over Baseline in individual symptom scores and quality of life using the LCSS

End point description:

The participant-reported LCSS was a 9-item questionnaire. Six items were symptom-specific measures for lung cancer (loss of appetite, fatigue, cough, dyspnea, hemoptysis, and pain), and 3 summation items described total symptomatic distress, interference with activity level, and global quality of life. Participant responses to each item were measured using VAS from 0 (for best outcome) to 100 (for worst outcome). The average symptom burden index (ASBI) was the mean of the 6 symptom-specific

items. The LCSS total score was the mean of the 9 items.

End point type	Secondary

End point timeframe:

Baseline through 30 days post discontinuation of study treatment (up to 39 Months)

End point values	Pemetrexed and BSC	Placebo and Best Supportive Care (BSC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	197		
Units: units on a scale				
arithmetic mean (standard deviation)				
Loss of appetite (n=403, 197)	7.3 (± 25.9)	10.6 (± 25.25)		
Fatigue (n=403, 197)	10.2 (± 27.1)	10.4 (± 23.92)		
Cough (n=402, 197)	7.6 (± 20.09)	6.7 (± 23.81)		
Dyspnea (n=400, 196)	7.6 (± 22.5)	5.4 (± 20.44)		
Pain (n=401, 197)	5.4 (± 20.96)	4.3 (± 21.93)		
Hemoptysis (n=402, 196)	1.5 (± 9.41)	2.1 (± 9.23)		
Symptom distress (n=401, 196)	6.5 (± 21.13)	8.2 (± 22.5)		
Interference with activity level (n=400, 197)	10.8 (± 27.08)	9.3 (± 25.5)		
Global quality of life (n=401, 195)	10.7 (± 24.94)	10.5 (± 22.98)		
ASBI (n=392, 195)	3.7 (± 12.34)	3.8 (± 13.24)		
Total LCSS (n=388, 193)	4.07 (± 12.76)	4.04 (± 13.03)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Entire Study	
Adverse event reporting additional description:	
H3E-MC-JMEN	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Pemetrexed
Reporting group description: -	

Serious adverse events	Placebo	Pemetrexed	
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 218 (14.22%)	83 / 438 (18.95%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
meningioma			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
metastases to central nervous system			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
tumour pain			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
pelvic venous thrombosis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
superior vena caval occlusion			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	4 / 438 (0.91%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
chest pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
death			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
fatigue			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
general physical health deterioration			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
mucosal inflammation			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
multi-organ failure			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
performance status decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

pyrexia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	4 / 438 (0.91%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
balanitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed[1]	0 / 158 (0.00%)	1 / 321 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
atelectasis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
bronchial obstruction			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cough			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
dyspnoea			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	6 / 218 (2.75%)	14 / 438 (3.20%)	
occurrences causally related to treatment / all	0 / 6	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 1	
haemoptysis			

alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoxia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pleural effusion			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia aspiration			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
pneumonitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary embolism			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary fibrosis			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
respiratory failure			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	4 / 438 (0.91%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Psychiatric disorders			
confusional state			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
weight decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
femur fracture			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
rib fracture			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
atrial fibrillation			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardiac failure			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardio-respiratory arrest			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
myocardial ischaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
myocardial infarction			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pericardial effusion			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

sinus tachycardia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
convulsion			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
dizziness			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
epilepsy			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
headache			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hemiparesis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoaesthesia			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ischaemic stroke			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
paraparesis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
paraplegia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
partial seizures			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
spinal cord compression			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
transient ischaemic attack			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	6 / 438 (1.37%)	
occurrences causally related to treatment / all	0 / 0	7 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
anaemia of malignant disease			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
febrile neutropenia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	4 / 438 (0.91%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
leukopenia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
neutropenia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	2 / 438 (0.46%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
thrombocytopenia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
vertigo			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
constipation			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
dysphagia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
haematemesis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
large intestine perforation			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
nausea			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
reflux oesophagitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
vomiting			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
dysuria			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
nephrolithiasis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
renal failure			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
renal failure acute			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary retention			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
back pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
bone pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
intervertebral disc degeneration			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
joint effusion			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
muscle contracture			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
muscular weakness			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
myalgia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pain in extremity			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	2 / 438 (0.46%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
bronchopneumonia			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cellulitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
erysipelas			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastrointestinal infection			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
herpes zoster			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
infection			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
oral candidiasis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

pneumonia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	3 / 218 (1.38%)	10 / 438 (2.28%)	
occurrences causally related to treatment / all	0 / 3	3 / 10	
deaths causally related to treatment / all	0 / 0	0 / 1	
pulmonary sepsis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
respiratory tract infection			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
sepsis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
skin infection			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary tract infection			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	3 / 438 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
urosepsis			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
viral upper respiratory tract infection			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
anorexia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	4 / 438 (0.91%)	
occurrences causally related to treatment / all	0 / 0	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
dehydration			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
diabetic ketoacidosis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypercalcaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypercholesterolaemia			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoglycaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

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

Non-serious adverse events	Placebo	Pemetrexed	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	178 / 218 (81.65%)	386 / 438 (88.13%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
angiolipoma			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
cancer pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	4 / 218 (1.83%)	11 / 438 (2.51%)	
occurrences (all)	4	11	
metastatic pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
neoplasm			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
oesophageal carcinoma			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
tumour pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	5 / 218 (2.29%)	5 / 438 (1.14%)	
occurrences (all)	5	5	
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
flushing			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	5 / 218 (2.29%)	8 / 438 (1.83%)	
occurrences (all)	7	10	
haemorrhage			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
hot flush			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	2 / 438 (0.46%)	
occurrences (all)	1	2	
hypertension			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	4 / 218 (1.83%)	11 / 438 (2.51%)	
occurrences (all)	4	11	
hypotension			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	3 / 218 (1.38%)	6 / 438 (1.37%)	
occurrences (all)	3	6	
orthostatic hypotension			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	1	
peripheral ischaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
phlebitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
shock			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
superior vena caval occlusion			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	3 / 438 (0.68%)	
occurrences (all)	1	3	
thrombosis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	3 / 438 (0.68%)	
occurrences (all)	2	3	
Surgical and medical procedures			
medical device implantation			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
pneumatic compression therapy			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
tumour excision			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	10 / 218 (4.59%)	48 / 438 (10.96%)	
occurrences (all)	11	74	
axillary pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
catheter site erythema			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
chest discomfort			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences (all)	0	14	
chest pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	16 / 218 (7.34%)	44 / 438 (10.05%)	
occurrences (all)	17	67	
chills			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	7 / 438 (1.60%)	
occurrences (all)	0	9	
condition aggravated			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
cyst			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
extravasation			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
face oedema			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	6 / 438 (1.37%)	
occurrences (all)	2	7	
facial pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
fatigue			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	49 / 218 (22.48%)	145 / 438 (33.11%)	
occurrences (all)	63	227	
feeling abnormal			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
gait disturbance			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
general physical health deterioration			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	7 / 438 (1.60%)	
occurrences (all)	0	9	
influenza like illness			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	3 / 218 (1.38%)	10 / 438 (2.28%)	
occurrences (all)	4	17	

injection site reaction			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	4 / 438 (0.91%)	
occurrences (all)	0	4	
irritability			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
localised oedema			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	4 / 438 (0.91%)	
occurrences (all)	0	4	
malaise			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	4	
mucosal inflammation			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	12 / 438 (2.74%)	
occurrences (all)	2	19	
obstruction			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
oedema			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	12 / 438 (2.74%)	
occurrences (all)	1	16	
oedema peripheral			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	27 / 438 (6.16%)	
occurrences (all)	3	34	
pain			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	13 / 218 (5.96%)	24 / 438 (5.48%)	
occurrences (all)	13	28	
peripheral coldness			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
pyrexia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	25 / 218 (11.47%)	56 / 438 (12.79%)	
occurrences (all)	33	78	
swelling			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
visceral oedema			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
Immune system disorders			
contrast media allergy			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
hypersensitivity			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	6 / 438 (1.37%)	
occurrences (all)	1	8	
seasonal allergy			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
balanitis			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed[2]	0 / 158 (0.00%)	1 / 321 (0.31%)	
occurrences (all)	0	1	
breast swelling			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
pelvic pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	1	
testicular disorder			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed[3]	0 / 158 (0.00%)	1 / 321 (0.31%)	
occurrences (all)	0	1	
testicular pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed[4]	0 / 158 (0.00%)	1 / 321 (0.31%)	
occurrences (all)	0	1	
vaginal haemorrhage			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed[5]	0 / 60 (0.00%)	2 / 117 (1.71%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
atelectasis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
bronchial obstruction			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
cough			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	47 / 218 (21.56%)	95 / 438 (21.69%)	
occurrences (all)	50	118	
dysphonia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	4 / 218 (1.83%)	2 / 438 (0.46%)	
occurrences (all)	4	2	
dyspnoea			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	43 / 218 (19.72%)	98 / 438 (22.37%)	
occurrences (all)	45	118	
dyspnoea exertional			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	2 / 438 (0.46%)	
occurrences (all)	1	2	
epistaxis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	5 / 438 (1.14%)	
occurrences (all)	1	8	
haemoptysis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	10 / 218 (4.59%)	24 / 438 (5.48%)	
occurrences (all)	11	26	
hiccups			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	3 / 218 (1.38%)	9 / 438 (2.05%)	
occurrences (all)	3	17	
hypoxia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences (all)	0	3	
pharyngolaryngeal pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	5 / 218 (2.29%)	10 / 438 (2.28%)	
occurrences (all)	5	11	

pleural effusion			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
pleurisy			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
pleuritic pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
pneumonitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
postnasal drip			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences (all)	0	5	
productive cough			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	3 / 218 (1.38%)	11 / 438 (2.51%)	
occurrences (all)	3	15	
pulmonary embolism			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
pulmonary haemorrhage			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	3 / 218 (1.38%)	0 / 438 (0.00%)	
occurrences (all)	3	0	
rales			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
rhinitis allergic			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	4 / 438 (0.91%)	
occurrences (all)	1	7	
rhinorrhoea			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	6 / 438 (1.37%)	
occurrences (all)	0	6	
rhonchi			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
wheezing			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	4 / 438 (0.91%)	
occurrences (all)	1	4	
Psychiatric disorders			
abnormal behaviour			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
agitation			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
anxiety			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	5 / 438 (1.14%)	
occurrences (all)	1	5	
confusional state			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	4 / 438 (0.91%)	
occurrences (all)	0	4	
depressed mood			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences (all)	0	3	
depression			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	9 / 438 (2.05%)	
occurrences (all)	1	9	
insomnia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	8 / 218 (3.67%)	28 / 438 (6.39%)	
occurrences (all)	8	31	
suicidal ideation			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
tic			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
Investigations			
alanine aminotransferase			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
alanine aminotransferase decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	1	
alanine aminotransferase increased			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	9 / 218 (4.13%)	60 / 438 (13.70%)	
occurrences (all)	11	87	
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	8 / 218 (3.67%)	52 / 438 (11.87%)	
occurrences (all)	10	63	
blood albumin decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
blood alkaline phosphatase			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	2	1	
blood alkaline phosphatase increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	4 / 218 (1.83%)	12 / 438 (2.74%)	
occurrences (all)	4	16	
blood bilirubin increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
blood bicarbonate decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
blood calcium decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
blood creatinine decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	3 / 438 (0.68%)	
occurrences (all)	1	10	

blood creatinine increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	4 / 218 (1.83%)	21 / 438 (4.79%)	
occurrences (all)	4	30	
blood fibrinogen increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
blood glucose increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	3	
blood iron decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
blood lactate dehydrogenase increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	9 / 438 (2.05%)	
occurrences (all)	1	15	
blood potassium decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
blood potassium increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	2	
blood sodium decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
blood sodium increased			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
blood uric acid increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
c-reactive protein increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	1	
creatinine renal clearance decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	18 / 438 (4.11%)	
occurrences (all)	2	28	
forced expiratory volume decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
gamma-glutamyltransferase increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	5 / 218 (2.29%)	6 / 438 (1.37%)	
occurrences (all)	5	7	
glomerular filtration rate			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	3	
glomerular filtration rate decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	5 / 438 (1.14%)	
occurrences (all)	0	10	
granulocyte count decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	

granulocyte count increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	2	0	
haemoglobin			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
haemoglobin decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	19 / 438 (4.34%)	
occurrences (all)	2	30	
neutrophil count decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	11 / 438 (2.51%)	
occurrences (all)	1	16	
neutrophil count increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences (all)	0	4	
platelet count			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
platelet count decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	5 / 438 (1.14%)	
occurrences (all)	2	5	
platelet count increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	1 / 438 (0.23%)	
occurrences (all)	3	1	
red blood cell count decreased			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	1 / 218 (0.46%)	2 / 438 (0.46%)	
occurrences (all)	1	5	
red blood cell microcytes present			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
renal function test abnormal			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	3	
sensory level			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
total bile acids increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
transaminases increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
troponin t			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
weight decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	3 / 218 (1.38%)	17 / 438 (3.88%)	
occurrences (all)	3	20	
weight increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	5 / 438 (1.14%)	
occurrences (all)	1	5	

white blood cell count decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	4 / 438 (0.91%)	
occurrences (all)	0	5	
white blood cell count increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	1 / 438 (0.23%)	
occurrences (all)	3	1	
Injury, poisoning and procedural complications			
arterial injury			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
contusion			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	3 / 438 (0.68%)	
occurrences (all)	1	3	
fall			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
foot fracture			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
fracture			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
incision site pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
procedural headache			
alternative dictionary used:			

MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
radiation skin injury			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	1	
rib fracture			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
thermal burn			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	1	
wound			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
Cardiac disorders			
arrhythmia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	1	
arrhythmia supraventricular			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
atrial fibrillation			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
atrial tachycardia			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	1	
bradycardia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
cyanosis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
myocardial ischaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
palpitations			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	3 / 218 (1.38%)	1 / 438 (0.23%)	
occurrences (all)	3	2	
pericardial effusion			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
sinus tachycardia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	1	
tachycardia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	3 / 438 (0.68%)	
occurrences (all)	1	4	
Nervous system disorders			
ageusia			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
aphonia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
aphasia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
ataxia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	5 / 438 (1.14%)	
occurrences (all)	0	6	
balance disorder			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
brain injury			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
burning sensation			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
cerebral ischaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	0 / 438 (0.00%)	
occurrences (all)	2	0	
cognitive disorder			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	2 / 438 (0.46%)	
occurrences (all)	1	2	

coma			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
convulsion			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	3 / 438 (0.68%)	
occurrences (all)	1	3	
depressed level of consciousness			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
disturbance in attention			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
dizziness			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	7 / 218 (3.21%)	34 / 438 (7.76%)	
occurrences (all)	7	39	
dysgeusia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	10 / 438 (2.28%)	
occurrences (all)	1	14	
dysaesthesia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	2	
dysphasia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
formication			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
headache			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	19 / 218 (8.72%)	51 / 438 (11.64%)	
occurrences (all)	26	62	
hemicephalalgia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
hemiparesis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
hypoaesthesia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	3 / 218 (1.38%)	5 / 438 (1.14%)	
occurrences (all)	3	6	
memory impairment			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
neuralgia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	4 / 438 (0.91%)	
occurrences (all)	1	4	
neuropathy peripheral			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	10 / 438 (2.28%)	
occurrences (all)	2	11	
neurotoxicity			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	

paraesthesia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	11 / 218 (5.05%)	27 / 438 (6.16%)	
occurrences (all)	12	29	
peripheral motor neuropathy			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
peripheral sensory neuropathy			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	6 / 218 (2.75%)	22 / 438 (5.02%)	
occurrences (all)	6	22	
poor quality sleep			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
somnolence			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
speech disorder			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
stupor			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
syncope			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	1	
syncope vasovagal			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
transient ischaemic attack			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
tremor			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences (all)	0	3	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	12 / 218 (5.50%)	65 / 438 (14.84%)	
occurrences (all)	15	97	
anaemia of malignant disease			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
febrile neutropenia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
leukocytosis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
leukopenia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	5 / 218 (2.29%)	25 / 438 (5.71%)	
occurrences (all)	8	64	
lymph node pain			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
lymphadenopathy			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences (all)	0	4	
lymphopenia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	3 / 438 (0.68%)	
occurrences (all)	1	3	
neutropenia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	5 / 218 (2.29%)	21 / 438 (4.79%)	
occurrences (all)	5	66	
neutrophilia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
thrombocythaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
thrombocytopenia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	17 / 438 (3.88%)	
occurrences (all)	3	29	
Ear and labyrinth disorders			
cerumen impaction			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
deafness			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	3	
ear discomfort			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
ear pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
hypoacusis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
motion sickness			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
tinnitus			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	5 / 438 (1.14%)	
occurrences (all)	1	5	
vertigo			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	2 / 438 (0.46%)	
occurrences (all)	1	2	
Eye disorders			
blepharitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
cataract			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	1 / 218 (0.46%)	2 / 438 (0.46%)	
occurrences (all)	1	2	
conjunctivitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	20 / 438 (4.57%)	
occurrences (all)	1	24	
conjunctivitis allergic			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
dry eye			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	1	
eye pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
eye swelling			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
eyelid oedema			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences (all)	0	3	
keratoconjunctivitis sicca			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	4 / 438 (0.91%)	
occurrences (all)	0	4	
lacrimation increased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	20 / 438 (4.57%)	
occurrences (all)	0	21	

ocular surface disease			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	3 / 438 (0.68%)	
occurrences (all)	2	5	
photophobia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
pterygium			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
vision blurred			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	8 / 438 (1.83%)	
occurrences (all)	1	10	
visual acuity reduced			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	1	
visual disturbance			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
abdominal distension			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	4 / 438 (0.91%)	
occurrences (all)	2	4	
abdominal pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	8 / 218 (3.67%)	18 / 438 (4.11%)	
occurrences (all)	8	18	
abdominal pain lower			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
abdominal pain upper			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	3 / 218 (1.38%)	7 / 438 (1.60%)	
occurrences (all)	11	7	
aphthous stomatitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
ascites			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
constipation			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	17 / 218 (7.80%)	59 / 438 (13.47%)	
occurrences (all)	22	85	
dental caries			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
diarrhoea			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	15 / 218 (6.88%)	52 / 438 (11.87%)	
occurrences (all)	17	88	
dry mouth			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	3 / 218 (1.38%)	10 / 438 (2.28%)	
occurrences (all)	3	10	
dysphagia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	4 / 438 (0.91%)	
occurrences (all)	2	5	

dyspepsia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	6 / 218 (2.75%)	13 / 438 (2.97%)	
occurrences (all)	21	18	
faecal incontinence			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
faecaloma			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	0 / 438 (0.00%)	
occurrences (all)	2	0	
flatulence			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	4 / 438 (0.91%)	
occurrences (all)	0	7	
gastric disorder			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
gastritis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	4 / 438 (0.91%)	
occurrences (all)	1	5	
gastrointestinal pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	1 / 438 (0.23%)	
occurrences (all)	2	1	
gingival pain			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
gingivitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	1	
haemorrhoids			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
hiatus hernia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
ileus			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
inflammatory bowel disease			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
lip ulceration			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
mouth ulceration			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences (all)	0	3	
nausea			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	22 / 218 (10.09%)	102 / 438 (23.29%)	
occurrences (all)	24	209	

odynophagia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	4 / 438 (0.91%)	
occurrences (all)	1	5	
oesophageal haemorrhage			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
oesophagitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
oral pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	2 / 438 (0.46%)	
occurrences (all)	1	2	
paraesthesia oral			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	4	
periodontal disease			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
rectal haemorrhage			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	1	
stomatitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	19 / 438 (4.34%)	
occurrences (all)	1	22	
tongue black hairy			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
tongue coated			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
toothache			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	4 / 438 (0.91%)	
occurrences (all)	0	4	
vomiting			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	9 / 218 (4.13%)	56 / 438 (12.79%)	
occurrences (all)	12	88	
Hepatobiliary disorders			
cholelithiasis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
hepatic pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
hepatitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
hepatomegaly			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
hyperbilirubinaemia			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
acne			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	1 / 438 (0.23%)	
occurrences (all)	2	2	
alopecia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	21 / 438 (4.79%)	
occurrences (all)	1	23	
dermal cyst			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
dermatitis acneiform			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	4 / 218 (1.83%)	2 / 438 (0.46%)	
occurrences (all)	4	6	
dermatosis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	2	
dermatitis exfoliative			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
dry skin			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	5 / 438 (1.14%)	
occurrences (all)	1	6	
erythema			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
hyperhidrosis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	12 / 438 (2.74%)	
occurrences (all)	0	15	
madarosis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
nail disorder			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
night sweats			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	2 / 438 (0.46%)	
occurrences (all)	1	2	
pain of skin			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	0 / 438 (0.00%)	
occurrences (all)	2	0	
periorbital oedema			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
petechiae			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	5	
photosensitivity reaction			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	

pigmentation disorder			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	4 / 438 (0.91%)	
occurrences (all)	0	7	
pruritus			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	7 / 218 (3.21%)	18 / 438 (4.11%)	
occurrences (all)	8	22	
pruritus generalised			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
psoriasis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
rash			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	14 / 218 (6.42%)	62 / 438 (14.16%)	
occurrences (all)	16	81	
rash pruritic			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences (all)	0	3	
skin discolouration			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
skin exfoliation			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
skin hyperpigmentation			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	1 / 218 (0.46%)	9 / 438 (2.05%)	
occurrences (all)	1	9	
skin hypopigmentation			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
skin toxicity			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
swelling face			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
urticaria			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	4	
Renal and urinary disorders			
bladder spasm			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
calculus bladder			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
dysuria			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences (all)	0	8	
glycosuria			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
haematuria			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
haemorrhage urinary tract			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
incontinence			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
micturition urgency			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
nocturia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
pollakiuria			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences (all)	0	4	
renal failure			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences (all)	0	3	
urinary hesitation			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	3	

urinary incontinence			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	1 / 438 (0.23%)	
occurrences (all)	2	1	
urinary retention			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	5 / 438 (1.14%)	
occurrences (all)	0	5	
Endocrine disorders			
goitre			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
hyperthyroidism			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
hypothyroidism			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	7 / 218 (3.21%)	12 / 438 (2.74%)	
occurrences (all)	7	16	
arthritis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
back pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	8 / 218 (3.67%)	41 / 438 (9.36%)	
occurrences (all)	8	48	
bone pain			

alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	10 / 218 (4.59%)	14 / 438 (3.20%)	
occurrences (all)	10	14	
flank pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	2	
muscle spasms			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences (all)	0	3	
musculoskeletal chest pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	5 / 218 (2.29%)	8 / 438 (1.83%)	
occurrences (all)	5	8	
muscular weakness			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	5 / 438 (1.14%)	
occurrences (all)	2	6	
musculoskeletal discomfort			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
musculoskeletal pain			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	5 / 218 (2.29%)	12 / 438 (2.74%)	
occurrences (all)	6	14	
myalgia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	5 / 218 (2.29%)	15 / 438 (3.42%)	
occurrences (all)	7	17	
neck pain			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	5 / 218 (2.29%)	3 / 438 (0.68%)	
occurrences (all)	6	5	
pain in extremity			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	9 / 218 (4.13%)	11 / 438 (2.51%)	
occurrences (all)	11	14	
pain in jaw			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	7	
scleroderma			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
tendonitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
Infections and infestations			
abscess			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
bronchitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	15 / 438 (3.42%)	
occurrences (all)	2	17	
candidiasis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
cellulitis			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	2	
cystitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	3	
diverticulitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
ear infection			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
erysipelas			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
folliculitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
fungal infection			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
gastroenteritis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
gastroenteritis viral			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	

hepatic infection			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
herpes simplex			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
herpes virus infection			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
herpes zoster			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	3 / 438 (0.68%)	
occurrences (all)	1	3	
infection			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	3 / 218 (1.38%)	3 / 438 (0.68%)	
occurrences (all)	3	3	
influenza			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	10 / 438 (2.28%)	
occurrences (all)	0	12	
laryngitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	0 / 438 (0.00%)	
occurrences (all)	2	0	
lower respiratory tract infection			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
lung infection			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	1 / 218 (0.46%)	3 / 438 (0.68%)	
occurrences (all)	1	3	
nasopharyngitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	3 / 218 (1.38%)	14 / 438 (3.20%)	
occurrences (all)	3	17	
oral candidiasis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	4 / 438 (0.91%)	
occurrences (all)	0	4	
oral herpes			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	0 / 438 (0.00%)	
occurrences (all)	2	0	
otitis media			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
paronychia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
parotitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
pharyngitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
pneumonia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	2 / 438 (0.46%)	
occurrences (all)	2	2	

pyothorax			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
respiratory tract infection			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
respiratory tract infection viral			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
rhinitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
sinusitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences (all)	0	3	
soft tissue infection			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
tonsillitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
tooth abscess			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
tooth infection			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
upper respiratory tract infection			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	3 / 218 (1.38%)	15 / 438 (3.42%)	
occurrences (all)	3	20	
urinary tract infection			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	4 / 218 (1.83%)	5 / 438 (1.14%)	
occurrences (all)	4	7	
Metabolism and nutrition disorders			
acidosis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
alcohol intolerance			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
alkalosis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
anorexia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	40 / 218 (18.35%)	124 / 438 (28.31%)	
occurrences (all)	43	238	
dehydration			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	7 / 438 (1.60%)	
occurrences (all)	1	8	
diabetes mellitus			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 218 (0.00%)	3 / 438 (0.68%)	
occurrences (all)	0	3	
fluid retention			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	3	
glucose tolerance impaired			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
hypercalcaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 218 (0.92%)	3 / 438 (0.68%)	
occurrences (all)	3	3	
hypercholesterolaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	1 / 438 (0.23%)	
occurrences (all)	1	2	
hypercreatininaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	
hyperglycaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	6 / 218 (2.75%)	18 / 438 (4.11%)	
occurrences (all)	7	20	
hyperkalaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	4 / 438 (0.91%)	
occurrences (all)	1	6	
hyperlipidaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	1 / 438 (0.23%)	
occurrences (all)	0	1	

hypernatraemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	3	
hypertriglyceridaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	1	0	
hyperuricaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	3 / 218 (1.38%)	1 / 438 (0.23%)	
occurrences (all)	3	1	
hypoalbuminaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	2 / 438 (0.46%)	
occurrences (all)	1	3	
hypocalcaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	2 / 438 (0.46%)	
occurrences (all)	0	2	
hypokalaemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	4 / 438 (0.91%)	
occurrences (all)	2	4	
hyponatraemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 218 (0.00%)	7 / 438 (1.60%)	
occurrences (all)	0	7	
hypophosphataemia			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 218 (0.46%)	0 / 438 (0.00%)	
occurrences (all)	2	0	
increased appetite			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed occurrences (all)	0 / 218 (0.00%) 0	1 / 438 (0.23%) 1	

Notes:

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 February 2007	Protocol H3E-MC-JMEN was amended to change the primary objective from Overall Survival (OS) to Progression Free Survival.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Four participants (pts) assigned to placebo received pemetrexed; pts analyzed for efficacy as randomized. Three treated pts did not sign ICF, 1 treated pt signed ICF but did not complete entire randomization process; pts excluded from all analyses.

Notes: