



Clinical trial results:

A Multicenter, Randomized, Double-Blind, Phase 3 Study of Ramucirumab (IMC-1121B) Drug Product and Best Supportive Care (BSC) Versus Placebo and BSC as Second-Line Treatment in Patients With Hepatocellular Carcinoma Following First-Line Therapy With Sorafenib (REACH)

Summary

EudraCT number	2010-019318-26
Trial protocol	FI DE CZ PT BE ES AT FR BG HU IT SE NO
Global end of trial date	17 March 2015

Results information

Result version number	v1 (current)
This version publication date	02 April 2016
First version publication date	02 April 2016

Trial information

Trial identification

Sponsor protocol code	I4T-IE-JVBF
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01140347
WHO universal trial number (UTN)	-
Other trial identifiers	Sponsor Trial Number: 13895, Sponsor Trial Alias: I4T-IE-JVBF, Alternate Trial Number: IMC-1121B

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Mon - Fri 9 AM - 5 PM Eastern time (UTC/GMT - 5 hours, EST), Eli Lilly and Company, 1 877-CTLilly,
Scientific contact	Mon - Fri 9 AM - 5 PM Eastern time (UTC/GMT - 5 hours, 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	17 March 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	17 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to compare the overall survival (OS; time from randomization to death) in participants with hepatocellular carcinoma (HCC) who had disease progression during or following sorafenib therapy, or were intolerant to this agent. Participants will receive either ramucirumab (IMC 1121B) plus best supportive care (BSC) or placebo plus BSC.

Protection of trial subjects:

This study was conducted in accordance with International Conference of Harmonization (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 was conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 October 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 37
Country: Number of subjects enrolled	Portugal: 2
Country: Number of subjects enrolled	Philippines: 1
Country: Number of subjects enrolled	Taiwan: 58
Country: Number of subjects enrolled	Hong Kong: 24
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	Thailand: 6
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	Italy: 51
Country: Number of subjects enrolled	France: 59
Country: Number of subjects enrolled	Australia: 11
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Korea, Republic of: 70
Country: Number of subjects enrolled	Finland: 3
Country: Number of subjects enrolled	Austria: 8
Country: Number of subjects enrolled	Czech Republic: 20
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Canada: 1

Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Brazil: 27
Country: Number of subjects enrolled	Romania: 7
Country: Number of subjects enrolled	Bulgaria: 6
Country: Number of subjects enrolled	Germany: 40
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Japan: 93
Country: Number of subjects enrolled	Sweden: 2
Worldwide total number of subjects	565
EEA total number of subjects	233

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)	308
From 65 to 84 years	253
85 years and over	4

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants who died due to any cause or were alive and on study at conclusion but off treatment were considered to have completed the study.

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	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Ramucirumab + BSC

Arm description:

Ramucirumab: 8 milligrams/kilogram (mg/kg) intravenous (IV) infusion every 2 weeks.

Best supportive care (BSC): Palliative and supportive care for disease-related symptoms and toxicity associated with treatment as deemed medically necessary and appropriate in the opinion of the investigator.

Arm type	Experimental
Investigational medicinal product name	Ramucirumab
Investigational medicinal product code	
Other name	LY3009806, IMC-1121B
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

8 milligrams/kilogram (mg/kg) intravenous (IV) every 2 weeks

Arm title	Placebo + BSC
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Arm description:

Placebo: 8 mg/kg IV infusion every 2 weeks.

BSC: Palliative and supportive care for disease-related symptoms and toxicity associated with treatment as deemed medically necessary and appropriate in the opinion of the investigator.

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

Dosage and administration details:

8 mg/kg IV every 2 weeks

Number of subjects in period 1	Ramucirumab + BSC	Placebo + BSC
Started	283	282
Received at Least 1 Dose of Study Drug	277	276
Completed	265	268
Not completed	18	14
Consent withdrawn by subject	13	8
Lost to follow-up	5	6

Baseline characteristics

Reporting groups

Reporting group title	Ramucirumab + BSC
Reporting group description:	
Ramucirumab: 8 milligrams/kilogram (mg/kg) intravenous (IV) infusion every 2 weeks. Best supportive care (BSC): Palliative and supportive care for disease-related symptoms and toxicity associated with treatment as deemed medically necessary and appropriate in the opinion of the investigator.	
Reporting group title	Placebo + BSC
Reporting group description:	
Placebo: 8 mg/kg IV infusion every 2 weeks. BSC: Palliative and supportive care for disease-related symptoms and toxicity associated with treatment as deemed medically necessary and appropriate in the opinion of the investigator.	

Reporting group values	Ramucirumab + BSC	Placebo + BSC	Total
Number of subjects	283	282	282
Age categorical			
Unable to enter data due to EudraCT system limitation, see below for age categorical data.			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	62.9	62.5	
standard deviation	± 11.56	± 11.1	-
Gender categorical			
Unable to enter ramucirumab data due to EudraCT system limitation, see below for gender categorical data.			
Units: Subjects			
Male		242	242
Female		40	40
Ethnicity			
Units: Subjects			
Hispanic or Latino	23	20	43
Not Hispanic or Latino	253	260	513
Unknown or Not Reported	7	2	9
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	131	135	266
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	5	3	8
White	139	137	276
More than one race	0	0	0
Unknown or Not Reported	8	7	15
Region of Enrollment			
Units: Subjects			
United States	17	20	37
Portugal	0	2	2
Philippines	1	0	1

Taiwan	33	25	58
Hong Kong	14	10	24
Spain	9	12	21
Thailand	5	1	6
Israel	1	1	2
Switzerland	1	1	2
Italy	33	18	51
France	32	27	59
Australia	3	8	11
Netherlands	2	1	3
Korea, Republic of	28	42	70
Finland	0	3	3
Austria	4	4	8
Czech Republic	11	9	20
Hungary	1	0	1
Canada	0	1	1
Belgium	3	5	8
Brazil	15	12	27
Romania	3	4	7
Bulgaria	2	4	6
Germany	19	21	40
Norway	1	1	2
Japan	45	48	93
Sweden	0	2	2
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	149	159	308
From 65-84 years	131	122	253
85 years and over	3	1	4
Gender categorical			
Units: Subjects			
Male	236	242	478
Female	47	40	87

End points

End points reporting groups

Reporting group title	Ramucirumab + BSC
Reporting group description: Ramucirumab: 8 milligrams/kilogram (mg/kg) intravenous (IV) infusion every 2 weeks. Best supportive care (BSC): Palliative and supportive care for disease-related symptoms and toxicity associated with treatment as deemed medically necessary and appropriate in the opinion of the investigator.	
Reporting group title	Placebo + BSC
Reporting group description: Placebo: 8 mg/kg IV infusion every 2 weeks. BSC: Palliative and supportive care for disease-related symptoms and toxicity associated with treatment as deemed medically necessary and appropriate in the opinion of the investigator.	

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description: OS was defined as the time from the date of randomization to the date of death from any cause. Participants who were alive at the end of the follow-up period or were lost to follow-up were censored on the last date the participant was known to be alive.	
End point type	Primary
End point timeframe: Randomization to death from any cause (up to 37 months)	

End point values	Ramucirumab + BSC	Placebo + BSC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	283	282		
Units: months				
median (confidence interval 95%)	9.17 (8.05 to 10.64)	7.62 (6.01 to 9.33)		

Statistical analyses

Statistical analysis title	STATISTICAL ANALYSIS 1
Comparison groups	Placebo + BSC v Ramucirumab + BSC
Number of subjects included in analysis	565
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1391
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.866

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.717
upper limit	1.046

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)
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End point description:

PFS was defined as time from date of randomization until date of objectively determined progressive disease (PD) as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version (v) 1.1 or death from any cause. PD was defined as $\geq 20\%$ increase in sum of diameters (SOD) of target lesions, taking as reference smallest sum on study (including baseline sum if it was smallest). Sum must show a ≥ 5 millimeter (mm) increase. Appearance of ≥ 1 new lesions and unequivocal progression of existing non-target lesions were considered progression. In primary analysis, participants alive and without PD were censored at day of last adequate tumor assessment; progression or deaths without progression occurring immediately after ≥ 2 missed tumor assessments, were censored at day of the last adequate tumor assessment prior to missing assessments; participants who began new anticancer therapy were censored at day of the last adequate tumor assessment prior to start of new anticancer therapy.

End point type	Secondary
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End point timeframe:

Randomization to Progressive Disease (PD) (up to 36 months)

End point values	Ramucirumab + BSC	Placebo + BSC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	283	282		
Units: months				
median (confidence interval 95%)	2.79 (2.69 to 3.94)	2.1 (1.58 to 2.69)		

Statistical analyses

Statistical analysis title	STATISTICAL ANALYSIS 1
Comparison groups	Placebo + BSC v Ramucirumab + BSC
Number of subjects included in analysis	565
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.625
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.522
upper limit	0.75

Secondary: Percentage of Participants with Complete Response (CR) or Partial Response (PR) [Objective Response Rate (ORR)]

End point title	Percentage of Participants with Complete Response (CR) or Partial Response (PR) [Objective Response Rate (ORR)]
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End point description:

ORR was defined, using RECIST v1.1 criteria, as the percentage of participants who achieved a best overall response of CR or PR. CR was defined as the disappearance of all lesions and any intratumor arterial enhancement in target lesions, the normalization of the tumor marker level and all lymph nodes short axis reduced to <10 mm. PR was defined as $\geq 30\%$ decrease in the SOD of target lesions, including the short axes of any target lymph nodes, taking as reference the baseline SOD of target lesions, no new lesions and stable nontarget lesions. Percentage of participants was calculated as: (number of participants with CR or PR / number of participants randomized) * 100.

End point type	Secondary
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End point timeframe:

Baseline to the date of first evidence of confirmed CR or PR (up to 37 months)

End point values	Ramucirumab + BSC	Placebo + BSC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	283	282		
Units: percentage of participants				
number (confidence interval 95%)	7.1 (4.6 to 10.7)	0.7 (0.2 to 2.5)		

Statistical analyses

Statistical analysis title	STATISTICAL ANALYSIS 1
Comparison groups	Placebo + BSC v Ramucirumab + BSC
Number of subjects included in analysis	565
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 ^[1]
Method	Cochran-Mantel-Haenszel
Confidence interval	
sides	2-sided

Notes:

[1] - Cochran-Mantel-Haenszel (CMH) adjusted for geographic region and etiology liver disease.

Secondary: Time to Radiographic Progression (TTP)

End point title	Time to Radiographic Progression (TTP)
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End point description:

TTP was defined as the time from randomization to the first radiographically documented PD. PD was defined, using RECIST v1.1 criteria, as $\geq 20\%$ increase in SOD of target lesions, taking as reference smallest sum on study (including baseline sum if it was the smallest). Sum must show an absolute increase of ≥ 5 mm. Appearance of ≥ 1 new lesions and unequivocal progression of existing non-target lesions were considered progression. Participants without PD were censored at the day of the last

adequate tumor assessment. Progression occurred immediately after ≥ 2 missed tumor assessments and were censored at the day of the last adequate tumor assessment prior to the missing assessments. Participants who began new anticancer therapy were censored at the day of their last adequate tumor assessment prior to start of new anticancer therapy.

End point type	Secondary
End point timeframe:	
Randomization to PD (up to 36 months)	

End point values	Ramucirumab + BSC	Placebo + BSC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	283	282		
Units: months				
median (confidence interval 95%)	3.48 (2.76 to 4.47)	2.63 (1.58 to 2.76)		

Statistical analyses

Statistical analysis title	STATISTICAL ANALYSIS 1
Comparison groups	Placebo + BSC v Ramucirumab + BSC
Number of subjects included in analysis	565
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.593
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.487
upper limit	0.722

Secondary: Change from Baseline in the Functional Assessment of Cancer Therapy (FACT) Hepatobiliary Symptom Index-8 (FHSI-8)

End point title	Change from Baseline in the Functional Assessment of Cancer Therapy (FACT) Hepatobiliary Symptom Index-8 (FHSI-8)
End point description:	
The FHSI-8 is a self-administered 8-item questionnaire that measures a participant's symptoms in the domains of jaundice, stomach pain/discomfort weight loss, and fatigue. Participants rated each item on a 5-point scale from 0 (not at all) to 4 (very much). Item scores were calculated as outlined in the FACIT manual. FHSI-8 total score was the sum of each item's score with a total score ranging from 0 (highly symptomatic) to 32 (asymptomatic).	
End point type	Secondary
End point timeframe:	
Baseline, Prior to infusion on Day 1 of Cycle 4, Cycle 10, and Cycle 16 (14-day cycles), and end of treatment (up to 34 months)	

End point values	Ramucirumab + BSC	Placebo + BSC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169	199		
Units: units on a scale				
arithmetic mean (standard deviation)				
Cycle 4 (n=166, 147)	-1.26 (± 3.164)	-0.81 (± 4.623)		
Cycle 10 (n=70, 45)	-1.28 (± 3.989)	-0.01 (± 4.378)		
Cycle 16 (n=47, 24)	-0.97 (± 4.095)	0.75 (± 3.768)		
End of Treatment (n=169, 199)	-2.44 (± 5.561)	-2.86 (± 5.618)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in European Quality of Life Questionnaire-5 Dimensions (EQ-5D) Health State Score

End point title	Change from Baseline in European Quality of Life Questionnaire-5 Dimensions (EQ-5D) Health State Score
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End point description:

The EQ-5D is a self-reported, 5-dimension (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) questionnaire related to the participant's current health state. Each question was scored using a 3 level scale (no problems, some problems, or extreme problems). EQ-5D health state was defined by combining responses from each of the 5 dimensions into a weighted health-state index score according to the United Kingdom (UK) population based algorithm where 0 = death and 1 = perfect health.

End point type	Secondary
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End point timeframe:

Baseline, Prior to Infusion on Day 1 of Cycle 4, Cycle 10, and Cycle 16 (14-day cycles), end of treatment (up to 34 months)

End point values	Ramucirumab + BSC	Placebo + BSC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	166	190		
Units: units on a scale				
arithmetic mean (standard deviation)				
Cycle 4 (n=166, 145)	-0.038 (± 0.189)	-0.046 (± 0.245)		
Cycle 10 (n=71, 45)	-0.054 (± 0.212)	0.003 (± 0.148)		
Cycle 16 (n=47, 25)	-0.062 (± 0.214)	-0.012 (± 0.085)		

End of Treatment (n=166, 190)	-0.129 (± 0.29)	-0.144 (± 0.28)		
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Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events (AEs) and the Number of Participants Who Died

End point title	Number of Participants with Adverse Events (AEs) and the Number of Participants Who Died
End point description: The number of participants with serious AEs (SAEs), other non-serious AEs and participants who died. A summary of SAEs 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 37 months)	

End point values	Ramucirumab + BSC	Placebo + BSC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	277	276		
Units: participants				
number (not applicable)				
SAEs	123	92		
Other Non-SAEs	254	235		
Died	215	220		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Concentration (Cmax) of Ramucirumab, Cycle 1

End point title	Maximum Concentration (Cmax) of Ramucirumab, Cycle 1 ^[2]
End point description:	
End point type	Secondary
End point timeframe: 1 hour following the completion of Cycle 1 (14-day cycle) infusion	

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic assays are only performed on specimens from participants with exposure to study drug.

End point values	Ramucirumab + BSC			
Subject group type	Reporting group			
Number of subjects analysed	247			
Units: micrograms/milliliter (µg/mL)				
geometric mean (geometric coefficient of variation)	149.6 (± 36.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of Ramucirumab, Cycle 4

End point title	Cmax of Ramucirumab, Cycle 4 ^[3]
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End point description:

End point type	Secondary
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End point timeframe:

1 hour following completion of Cycle 4 (14-day cycles) infusion

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Pharmacokinetic assays are only performed on specimens from participants with exposure to study drug.

End point values	Ramucirumab + BSC			
Subject group type	Reporting group			
Number of subjects analysed	140			
Units: µg/mL				
geometric mean (geometric coefficient of variation)	189.5 (± 39.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of Ramucirumab, Cycle 7

End point title	Cmax of Ramucirumab, Cycle 7 ^[4]
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End point description:

End point type	Secondary
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End point timeframe:

1 hour following completion of Cycle 7 (14-day cycles) infusion

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Pharmacokinetic assays are only performed on specimens from participants with exposure to study drug.

End point values	Ramucirumab + BSC			
Subject group type	Reporting group			
Number of subjects analysed	81			
Units: µg/mL				
geometric mean (geometric coefficient of variation)	184.4 (± 56.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment-Emergent Positive Anti-Ramucirumab Response [Serum Anti-Ramucirumab Antibody Assessment (Immunogenicity)]

End point title	Number of Participants with Treatment-Emergent Positive Anti-Ramucirumab Response [Serum Anti-Ramucirumab Antibody Assessment (Immunogenicity)]
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End point description:

Participants were considered positive for anti-ramucirumab antibodies [anti-drug antibodies (ADA)] if the post-treatment sample had an increase of at least 4-fold in titer from the pretreatment values. If the pretreatment value was not detected or was not present, a 1:20 post-treatment titer was required to indicate treatment emergence of ADA.

End point type	Secondary
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End point timeframe:

Prior to treatment and 1 hour post end of infusion for Cycles 1, 4 and 7 (14-day cycles)

End point values	Ramucirumab + BSC	Placebo + BSC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	231		
Units: participants				
number (not applicable)	10	7		

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:

Safety population includes any participants who received at least 1 dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	Ramucirumab 8 mg/kg I.V. infusion every 2 weeks
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Reporting group description: -

Reporting group title	Placebo 8 mg/kg I.V. infusion every 2 weeks
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Reporting group description: -

Serious adverse events	Ramucirumab 8 mg/kg I.V. infusion every 2 weeks	Placebo 8 mg/kg I.V. infusion every 2 weeks	
Total subjects affected by serious adverse events			
subjects affected / exposed	124 / 277 (44.77%)	92 / 276 (33.33%)	
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)			
liver carcinoma ruptured			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	2 / 276 (0.72%)	
occurrences causally related to treatment / all	1 / 3	1 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
malignant neoplasm progression			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	23 / 277 (8.30%)	16 / 276 (5.80%)	
occurrences causally related to treatment / all	0 / 30	0 / 22	
deaths causally related to treatment / all	0 / 17	0 / 14	
metastases to bone			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
metastases to central nervous system			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
metastases to lung			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
small intestine adenocarcinoma			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
tumour associated fever			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
tumour pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	4 / 276 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
haemorrhage			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypertension			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
shock haemorrhagic			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 277 (1.44%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	1 / 5	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
chills			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
death			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
extravasation			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
fatigue			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	2 / 276 (0.72%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
general physical health deterioration			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	9 / 277 (3.25%)	3 / 276 (1.09%)	
occurrences causally related to treatment / all	2 / 9	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
generalised oedema			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hernia obstructive			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hyperthermia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

malaise			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
multi-organ failure			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	1 / 1	0 / 1	
non-cardiac chest pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
oedema			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
oedema peripheral			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pyrexia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	7 / 277 (2.53%)	3 / 276 (1.09%)	
occurrences causally related to treatment / all	2 / 8	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
sudden death			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
anaphylactic reaction			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
acute respiratory distress syndrome			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
dyspnoea			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	2 / 276 (0.72%)	
occurrences causally related to treatment / all	0 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
haemoptysis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoxia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pleural effusion			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	2 / 277 (0.72%)	3 / 276 (1.09%)	
occurrences causally related to treatment / all	0 / 2	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonitis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary embolism			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	2 / 276 (0.72%)	
occurrences causally related to treatment / all	0 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
pulmonary haemorrhage			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
mental status changes			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
blood bilirubin increased			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
blood creatinine increased alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
general physical condition abnormal alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
liver function test abnormal alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
fall alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
femur fracture alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
infusion related reaction alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
cardiac failure			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
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 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
supraventricular tachycardia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
central nervous system lesion			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cerebral infarction			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
coma hepatic			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
convulsion			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
diplegia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
dizziness			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
encephalopathy			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hepatic encephalopathy			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	12 / 277 (4.33%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	8 / 16	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
mental impairment			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

peripheral motor neuropathy alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
somnolence alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
spinal cord compression alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
subarachnoid haemorrhage alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
tongue biting alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
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 16.1			
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
disseminated intravascular coagulation alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
neutropenia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
thrombocytopenia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
retinal detachment			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (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 distension			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
abdominal pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	6 / 277 (2.17%)	9 / 276 (3.26%)	
occurrences causally related to treatment / all	1 / 7	1 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
abdominal pain upper			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ascites			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	8 / 277 (2.89%)	3 / 276 (1.09%)	
occurrences causally related to treatment / all	0 / 8	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
colitis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
diarrhoea			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
duodenal ulcer			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
dysphagia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
food poisoning			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

gastric antral vascular ectasia alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastric haemorrhage alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastric varices haemorrhage alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastroduodenitis alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastrointestinal haemorrhage alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	7 / 277 (2.53%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	5 / 7	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
haemorrhoids alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ileus alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
inguinal hernia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
intestinal obstruction			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
irritable bowel syndrome			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
large intestine perforation			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
melaena			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
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 16.1			
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

oesophageal haemorrhage alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
oesophageal varices haemorrhage alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 277 (1.44%)	10 / 276 (3.62%)	
occurrences causally related to treatment / all	1 / 5	7 / 12	
deaths causally related to treatment / all	0 / 1	1 / 1	
pancreatitis alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
peritoneal haemorrhage alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
small intestinal obstruction alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
umbilical hernia alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
upper gastrointestinal haemorrhage alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
varices oesophageal			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
vomiting			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
acute hepatic failure			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
bile duct stone			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cholangitis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	5 / 277 (1.81%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 8	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cholangitis acute			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hepatic cirrhosis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hepatic failure			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	6 / 277 (2.17%)	5 / 276 (1.81%)	
occurrences causally related to treatment / all	5 / 9	0 / 9	
deaths causally related to treatment / all	2 / 4	0 / 5	
hepatic function abnormal			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hepatorenal syndrome			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 277 (1.44%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	1 / 4	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
hyperbilirubinaemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	3 / 276 (1.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypertransaminasaemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

jaundice alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 277 (0.36%) 0 / 1 0 / 0	 1 / 276 (0.36%) 0 / 1 0 / 0	
jaundice cholestatic alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 277 (0.00%) 0 / 0 0 / 0	 2 / 276 (0.72%) 0 / 2 0 / 0	
liver disorder alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 277 (0.36%) 1 / 1 0 / 0	 0 / 276 (0.00%) 0 / 0 0 / 0	
portal vein thrombosis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 277 (0.36%) 0 / 1 0 / 0	 1 / 276 (0.36%) 1 / 1 0 / 0	
Skin and subcutaneous tissue disorders			
dermatitis allergic alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 277 (0.36%) 0 / 1 0 / 0	 0 / 276 (0.00%) 0 / 0 0 / 0	
skin lesion alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 277 (0.36%) 1 / 1 0 / 0	 0 / 276 (0.00%) 0 / 0 0 / 0	
skin ulcer alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
renal failure			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
renal failure acute			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	3 / 277 (1.08%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	2 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
renal impairment			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
arthritis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (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 16.1			
subjects affected / exposed	0 / 277 (0.00%)	4 / 276 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
flank pain			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
musculoskeletal chest pain alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
neck pain alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pathological fracture alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
spinal pain alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
anal abscess alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
bacteraemia alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
campylobacter infection			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
candida sepsis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
device related infection			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
device related sepsis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
infection			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
influenza			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

liver abscess				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
lobar pneumonia				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
lung infection				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)		
occurrences causally related to treatment / all	0 / 2	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
peritonitis				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)		
occurrences causally related to treatment / all	0 / 1	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
peritonitis bacterial				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
pneumonia				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	3 / 277 (1.08%)	3 / 276 (1.09%)		
occurrences causally related to treatment / all	1 / 3	1 / 4		
deaths causally related to treatment / all	0 / 0	0 / 1		
pneumonia bacterial				
alternative dictionary used: MedDRA 16.1				

subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia klebsiella			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary sepsis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
sepsis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	3 / 277 (1.08%)	2 / 276 (0.72%)	
occurrences causally related to treatment / all	1 / 3	1 / 3	
deaths causally related to treatment / all	1 / 2	0 / 1	
septic shock			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
upper respiratory tract infection			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary tract infection			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	3 / 277 (1.08%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	

Metabolism and nutrition disorders			
cachexia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
decreased appetite			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	3 / 277 (1.08%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
dehydration			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
diabetes mellitus			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypercalcaemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hyperglycaemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
hyperkalaemia			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypertriglyceridaemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypocalcaemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (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 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hyponatraemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Ramucirumab 8 mg/kg I.V. infusion every 2 weeks	Placebo 8 mg/kg I.V. infusion every 2 weeks	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	265 / 277 (95.67%)	257 / 276 (93.12%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
cancer pain			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	3 / 276 (1.09%)
occurrences (all)	1	3
haemangioma		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
haemangioma of skin		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	2	0
keratoacanthoma		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
malignant neoplasm progression		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	5 / 277 (1.81%)	3 / 276 (1.09%)
occurrences (all)	6	3
melanocytic naevus		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
metastases to lung		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	2	0
metastatic pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	2
pyogenic granuloma		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	2	0

<p>skin papilloma</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 277 (0.00%)</p> <p>0</p>	<p>1 / 276 (0.36%)</p> <p>1</p>	
<p>squamous cell carcinoma</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 277 (0.36%)</p> <p>1</p>	<p>0 / 276 (0.00%)</p> <p>0</p>	
<p>tongue neoplasm malignant stage unspecified</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 277 (0.00%)</p> <p>0</p>	<p>1 / 276 (0.36%)</p> <p>2</p>	
<p>tumour pain</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 277 (1.44%)</p> <p>4</p>	<p>4 / 276 (1.45%)</p> <p>5</p>	
<p>tumour thrombosis</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 277 (0.36%)</p> <p>1</p>	<p>0 / 276 (0.00%)</p> <p>0</p>	
<p>Vascular disorders</p> <p>deep vein thrombosis</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>embolism</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>extravasation blood</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>femoral artery occlusion</p> <p>alternative dictionary used:</p>	<p>1 / 277 (0.36%)</p> <p>1</p> <p>0 / 277 (0.00%)</p> <p>0</p> <p>1 / 277 (0.36%)</p> <p>1</p>	<p>1 / 276 (0.36%)</p> <p>1</p> <p>1 / 276 (0.36%)</p> <p>1</p> <p>1 / 276 (0.36%)</p> <p>1</p>	

MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
flushing		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	0 / 276 (0.00%)
occurrences (all)	3	0
haematoma		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	7 / 277 (2.53%)	2 / 276 (0.72%)
occurrences (all)	7	2
haemorrhage		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
hot flush		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	2
hypertension		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	55 / 277 (19.86%)	20 / 276 (7.25%)
occurrences (all)	104	43
hypotension		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	4 / 277 (1.44%)	4 / 276 (1.45%)
occurrences (all)	5	4
intermittent claudication		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
lymphostasis		
alternative dictionary used: MedDRA 16.1		

subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
orthostatic hypotension			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
peripheral coldness			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
periphlebitis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
thrombophlebitis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)	
occurrences (all)	3	0	
vein disorder			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
venous insufficiency			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	2 / 276 (0.72%)	
occurrences (all)	1	3	
venous lake			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
application site pain			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
asthenia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	50 / 277 (18.05%)	36 / 276 (13.04%)
occurrences (all)	80	63
axillary pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
catheter site pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	2	0
chest discomfort		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	3 / 276 (1.09%)
occurrences (all)	2	4
chest pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	8 / 276 (2.90%)
occurrences (all)	4	10
chills		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	11 / 277 (3.97%)	6 / 276 (2.17%)
occurrences (all)	15	15
crepitations		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	2	0
drug intolerance		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0

drug withdrawal syndrome		
alternative dictionary used:		
MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
effusion		
alternative dictionary used:		
MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
face oedema		
alternative dictionary used:		
MedDRA 16.1		
subjects affected / exposed	8 / 277 (2.89%)	1 / 276 (0.36%)
occurrences (all)	9	1
fatigue		
alternative dictionary used:		
MedDRA 16.1		
subjects affected / exposed	66 / 277 (23.83%)	60 / 276 (21.74%)
occurrences (all)	97	99
feeling cold		
alternative dictionary used:		
MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
gait disturbance		
alternative dictionary used:		
MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)
occurrences (all)	2	1
general physical health deterioration		
alternative dictionary used:		
MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	2 / 276 (0.72%)
occurrences (all)	2	2
generalised oedema		
alternative dictionary used:		
MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	4	0
hernia		
alternative dictionary used:		
MedDRA 16.1		

subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
hyperthermia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	0 / 276 (0.00%)
occurrences (all)	9	0
influenza like illness		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	6 / 277 (2.17%)	11 / 276 (3.99%)
occurrences (all)	9	25
infusion site pruritus		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
infusion site swelling		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
injection site reaction		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
injection site pruritus		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
local swelling		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	1 / 276 (0.36%)
occurrences (all)	4	2
localised oedema		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	3	0

malaise		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	5 / 277 (1.81%)	10 / 276 (3.62%)
occurrences (all)	6	11
medical device complication		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
mucosal dryness		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
mucosal inflammation		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	6 / 277 (2.17%)	3 / 276 (1.09%)
occurrences (all)	10	5
non-cardiac chest pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	7 / 276 (2.54%)
occurrences (all)	3	7
oedema		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	3 / 276 (1.09%)
occurrences (all)	3	6
oedema peripheral		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	100 / 277 (36.10%)	50 / 276 (18.12%)
occurrences (all)	151	58
pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	4 / 277 (1.44%)	5 / 276 (1.81%)
occurrences (all)	4	5
pyrexia		
alternative dictionary used: MedDRA 16.1		

subjects affected / exposed	42 / 277 (15.16%)	25 / 276 (9.06%)	
occurrences (all)	59	32	
suprapubic pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
systemic inflammatory response syndrome			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
thirst			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)	
occurrences (all)	2	0	
ulcer			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
xerosis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences (all)	1	1	
Immune system disorders			
cytokine release syndrome			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	3 / 277 (1.08%)	0 / 276 (0.00%)	
occurrences (all)	4	0	
hypersensitivity			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 277 (1.44%)	1 / 276 (0.36%)	
occurrences (all)	4	1	
seasonal allergy			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
balanitis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed ^[1]	1 / 230 (0.43%)	0 / 236 (0.00%)	
occurrences (all)	1	0	
benign prostatic hyperplasia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed ^[2]	1 / 230 (0.43%)	1 / 236 (0.42%)	
occurrences (all)	1	1	
breast pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 277 (1.44%)	1 / 276 (0.36%)	
occurrences (all)	5	1	
genital rash			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
gynaecomastia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed ^[3]	5 / 230 (2.17%)	0 / 236 (0.00%)	
occurrences (all)	6	0	
pelvic pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
pruritus genital			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	2	0	
rectocele			
alternative dictionary used: MedDRA 16.1			

<p>subjects affected / exposed^[4]</p> <p>occurrences (all)</p>	<p>1 / 47 (2.13%)</p> <p>1</p>	<p>0 / 40 (0.00%)</p> <p>0</p>	
<p>scrotal swelling</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed^[5]</p> <p>occurrences (all)</p>	<p>0 / 230 (0.00%)</p> <p>0</p>	<p>1 / 236 (0.42%)</p> <p>1</p>	
<p>sexual dysfunction</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 277 (0.00%)</p> <p>0</p>	<p>1 / 276 (0.36%)</p> <p>1</p>	
<p>Respiratory, thoracic and mediastinal disorders</p> <p>asthma</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 277 (0.00%)</p> <p>0</p>	<p>1 / 276 (0.36%)</p> <p>1</p>	
<p>atelectasis</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 277 (0.72%)</p> <p>2</p>	<p>1 / 276 (0.36%)</p> <p>1</p>	
<p>bronchial obstruction</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 277 (0.36%)</p> <p>1</p>	<p>0 / 276 (0.00%)</p> <p>0</p>	
<p>chronic obstructive pulmonary disease</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 277 (0.00%)</p> <p>0</p>	<p>1 / 276 (0.36%)</p> <p>1</p>	
<p>cough</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>41 / 277 (14.80%)</p> <p>54</p>	<p>25 / 276 (9.06%)</p> <p>29</p>	
<p>diaphragmalgia</p> <p>alternative dictionary used: MedDRA 16.1</p>			

subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
dysphonia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	9 / 277 (3.25%)	1 / 276 (0.36%)
occurrences (all)	9	2
dyspnoea		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	26 / 277 (9.39%)	26 / 276 (9.42%)
occurrences (all)	33	33
dyspnoea exertional		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	3 / 276 (1.09%)
occurrences (all)	5	3
epistaxis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	38 / 277 (13.72%)	17 / 276 (6.16%)
occurrences (all)	48	22
haemoptysis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	8 / 277 (2.89%)	2 / 276 (0.72%)
occurrences (all)	9	2
hiccups		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	6 / 277 (2.17%)	5 / 276 (1.81%)
occurrences (all)	7	6
hypoxia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
increased upper airway secretion		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0

interstitial lung disease			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
laryngeal inflammation			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
lung infiltration			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
nasal discomfort			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
nasal dryness			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
nasal mucosal disorder			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
oropharyngeal pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	6 / 277 (2.17%)	2 / 276 (0.72%)	
occurrences (all)	6	2	
pleural effusion			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	8 / 277 (2.89%)	9 / 276 (3.26%)	
occurrences (all)	11	11	
pleurisy			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
pneumonitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	2
productive cough		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	7 / 277 (2.53%)	5 / 276 (1.81%)
occurrences (all)	7	5
pulmonary artery thrombosis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
pulmonary congestion		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
pulmonary embolism		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
rales		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	4 / 277 (1.44%)	1 / 276 (0.36%)
occurrences (all)	4	1
rhinitis allergic		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	2 / 276 (0.72%)
occurrences (all)	1	2
rhinorrhoea		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	2 / 276 (0.72%)
occurrences (all)	2	2

<p>rhonchi</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 277 (0.36%)</p> <p>1</p>	<p>0 / 276 (0.00%)</p> <p>0</p>	
<p>sinus congestion</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 277 (0.36%)</p> <p>1</p>	<p>0 / 276 (0.00%)</p> <p>0</p>	
<p>tachypnoea</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 277 (0.00%)</p> <p>0</p>	<p>1 / 276 (0.36%)</p> <p>1</p>	
<p>upper-airway cough syndrome</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 277 (0.36%)</p> <p>1</p>	<p>0 / 276 (0.00%)</p> <p>0</p>	
<p>wheezing</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 277 (0.36%)</p> <p>1</p>	<p>0 / 276 (0.00%)</p> <p>0</p>	
<p>Psychiatric disorders</p> <p>abnormal dreams</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>agitation</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>anxiety</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>bulimia nervosa</p> <p>alternative dictionary used: MedDRA 16.1</p>	<p>0 / 277 (0.00%)</p> <p>0</p> <p>1 / 277 (0.36%)</p> <p>1</p> <p>2 / 277 (0.72%)</p> <p>2</p>	<p>1 / 276 (0.36%)</p> <p>1</p> <p>1 / 276 (0.36%)</p> <p>1</p> <p>7 / 276 (2.54%)</p> <p>18</p>	

subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
confusional state		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	8 / 277 (2.89%)	3 / 276 (1.09%)
occurrences (all)	9	3
delirium		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
depressed mood		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
depression		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	9 / 277 (3.25%)	1 / 276 (0.36%)
occurrences (all)	9	6
disorientation		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
insomnia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	19 / 277 (6.86%)	20 / 276 (7.25%)
occurrences (all)	20	20
mood altered		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
nightmare		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1

psychotic disorder alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
psychomotor retardation alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
Investigations			
activated partial thromboplastin time prolonged alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	2 / 276 (0.72%) 2	
alanine aminotransferase increased alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	13 / 277 (4.69%) 34	21 / 276 (7.61%) 33	
albumin urine present alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
alpha 1 foetoprotein increased alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	2 / 277 (0.72%) 2	1 / 276 (0.36%) 1	
ammonia increased alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	0 / 277 (0.00%) 0	1 / 276 (0.36%) 1	
aspartate aminotransferase increased alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	30 / 277 (10.83%) 59	39 / 276 (14.13%) 70	
biopsy liver			

alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
blood albumin decreased		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	8 / 277 (2.89%)	1 / 276 (0.36%)
occurrences (all)	37	1
blood alkaline phosphatase increased		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	18 / 277 (6.50%)	14 / 276 (5.07%)
occurrences (all)	40	25
blood bilirubin increased		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	19 / 277 (6.86%)	24 / 276 (8.70%)
occurrences (all)	39	38
blood chloride decreased		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	2
blood creatinine increased		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	5 / 277 (1.81%)	10 / 276 (3.62%)
occurrences (all)	15	12
blood chloride increased		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
blood lactate dehydrogenase increased		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)
occurrences (all)	2	1
blood magnesium decreased		
alternative dictionary used: MedDRA 16.1		

subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	2
blood potassium increased		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	2
blood pressure abnormal		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
blood pressure increased		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
blood urea increased		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	2
blood urine present		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	2	0
blood uric acid increased		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	4 / 277 (1.44%)	1 / 276 (0.36%)
occurrences (all)	7	1
body temperature increased		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	1 / 276 (0.36%)
occurrences (all)	4	1
breath sounds abnormal		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1

breath sounds			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
c-reactive protein increased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	3 / 276 (1.09%)	
occurrences (all)	1	4	
cd4 lymphocytes increased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
cardiac murmur			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)	
occurrences (all)	2	2	
coagulation time abnormal			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
ejection fraction decreased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
electrocardiogram qt prolonged			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)	
occurrences (all)	0	2	
electrocardiogram t wave inversion			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
gamma-glutamyltransferase increased			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	3 / 277 (1.08%)	6 / 276 (2.17%)
occurrences (all)	14	8
general physical condition abnormal		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	2
haematocrit decreased		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
haemoglobin decreased		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)
occurrences (all)	5	1
heart sounds abnormal		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
international normalised ratio increased		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	2 / 276 (0.72%)
occurrences (all)	2	2
lipase increased		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
liver function test abnormal		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	2 / 276 (0.72%)
occurrences (all)	2	2
mean cell volume decreased		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	2

monocyte count increased alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0
neutrophil count decreased alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 2	0 / 276 (0.00%) 0
occult blood alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0
platelet count decreased alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 2	1 / 276 (0.36%) 1
protein total decreased alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 3	0 / 276 (0.00%) 0
protein urine present alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	3 / 277 (1.08%) 7	0 / 276 (0.00%) 0
prothrombin time prolonged alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	0 / 277 (0.00%) 0	1 / 276 (0.36%) 1
sputum abnormal alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0
urine output decreased alternative dictionary used: MedDRA 16.1		

subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences (all)	1	1	
urine ketone body present			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
waist circumference increased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	2	0	
weight decreased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	9 / 277 (3.25%)	6 / 276 (2.17%)	
occurrences (all)	12	6	
weight increased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 277 (1.44%)	1 / 276 (0.36%)	
occurrences (all)	6	1	
white blood cell count decreased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	2	0	
white blood cells urine positive			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
anal injury			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
animal bite			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
chest injury		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
chillblains		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
clavicle fracture		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
contusion		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	4 / 277 (1.44%)	4 / 276 (1.45%)
occurrences (all)	4	4
craniocerebral injury		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
excoriation		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	3 / 276 (1.09%)
occurrences (all)	1	3
facial bones fracture		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
fall		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	7 / 277 (2.53%)	0 / 276 (0.00%)
occurrences (all)	8	0

foreign body			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
incision site pruritus			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
infusion related reaction			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	12 / 277 (4.33%)	1 / 276 (0.36%)	
occurrences (all)	13	1	
laceration			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
limb injury			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
lumbar vertebral fracture			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
postoperative wound complication			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
procedural pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)	
occurrences (all)	2	1	
rib fracture			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences (all)	1	1	
sternal fracture			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
sternal injury			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
stress fracture			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
tongue injury			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
tooth fracture			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences (all)	1	1	
wound			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)	
occurrences (all)	2	1	
wound haemorrhage			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
aortic valve incompetence			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
bradycardia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
bundle branch block right		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
cardiomyopathy		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
cyanosis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
myocardial infarction		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
palpitations		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	2 / 276 (0.72%)
occurrences (all)	2	2
sinus arrhythmia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
sinus tachycardia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0

supraventricular tachycardia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
tachycardia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	0 / 277 (0.00%) 0	1 / 276 (0.36%) 1	
tricuspid valve disease alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
Nervous system disorders ageusia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
amnesia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	4 / 277 (1.44%) 4	1 / 276 (0.36%) 1	
aphasia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	2 / 277 (0.72%) 2	0 / 276 (0.00%) 0	
aphonia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	0 / 277 (0.00%) 0	1 / 276 (0.36%) 1	
asterixis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
autonomic nervous system imbalance alternative dictionary used:			

MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
balance disorder		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	2	0
cerebral ischaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
circadian rhythm sleep disorder		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
clumsiness		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	2
consciousness fluctuating		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
convulsion		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)
occurrences (all)	2	1
diabetic neuropathy		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
disturbance in attention		
alternative dictionary used: MedDRA 16.1		

subjects affected / exposed	3 / 277 (1.08%)	0 / 276 (0.00%)
occurrences (all)	3	0
dizziness		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	23 / 277 (8.30%)	16 / 276 (5.80%)
occurrences (all)	25	18
dysaesthesia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
dysgeusia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	7 / 277 (2.53%)	3 / 276 (1.09%)
occurrences (all)	9	3
encephalopathy		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
headache		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	53 / 277 (19.13%)	15 / 276 (5.43%)
occurrences (all)	69	18
hemiparesis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
hepatic encephalopathy		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	9 / 277 (3.25%)	3 / 276 (1.09%)
occurrences (all)	10	3
hyperaesthesia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1

hypoesthesia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	3 / 277 (1.08%) 3	4 / 276 (1.45%) 5	
hypotonia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	0 / 277 (0.00%) 0	1 / 276 (0.36%) 1	
intercostal neuralgia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
lethargy alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	0 / 277 (0.00%) 0	1 / 276 (0.36%) 1	
loss of proprioception alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	0 / 277 (0.00%) 0	1 / 276 (0.36%) 1	
memory impairment alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	3 / 277 (1.08%) 3	0 / 276 (0.00%) 0	
movement disorder alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	0 / 277 (0.00%) 0	1 / 276 (0.36%) 1	
nervous system disorder alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
neuropathy peripheral alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	2 / 276 (0.72%)
occurrences (all)	1	2
paraesthesia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	8 / 277 (2.89%)	5 / 276 (1.81%)
occurrences (all)	14	6
parkinson's disease		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	2
peripheral sensory neuropathy		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	2 / 276 (0.72%)
occurrences (all)	2	2
petit mal epilepsy		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
polyneuropathy		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	2 / 276 (0.72%)
occurrences (all)	2	2
radiculitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
restless legs syndrome		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
sciatica		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	2

somnolence			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 277 (1.44%)	1 / 276 (0.36%)	
occurrences (all)	6	1	
spinal cord compression			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
status epilepticus			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
stupor			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
syncope			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)	
occurrences (all)	2	0	
transient ischaemic attack			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
tremor			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	3 / 276 (1.09%)	
occurrences (all)	1	3	
vocal cord paralysis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			

anaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	29 / 277 (10.47%)	31 / 276 (11.23%)
occurrences (all)	54	44
disseminated intravascular coagulation		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
eosinophilia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	2
hypochromic anaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	8	0
leukocytosis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	5 / 276 (1.81%)
occurrences (all)	3	5
leukopenia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	14 / 277 (5.05%)	7 / 276 (2.54%)
occurrences (all)	54	19
lymphopenia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	7 / 277 (2.53%)	4 / 276 (1.45%)
occurrences (all)	16	7
lymphadenopathy		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
neutropenia		
alternative dictionary used: MedDRA 16.1		

subjects affected / exposed	16 / 277 (5.78%)	4 / 276 (1.45%)	
occurrences (all)	80	8	
neutrophilia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
splenomegaly			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences (all)	1	1	
thrombocytopenia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	48 / 277 (17.33%)	12 / 276 (4.35%)	
occurrences (all)	189	26	
thrombocytosis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
deafness			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences (all)	1	1	
deafness neurosensory			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
ear congestion			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
ear discomfort			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
ear haemorrhage			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
hearing impaired			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)	
occurrences (all)	2	0	
tinnitus			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 277 (1.44%)	3 / 276 (1.09%)	
occurrences (all)	6	4	
vertigo			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 277 (1.44%)	5 / 276 (1.81%)	
occurrences (all)	4	8	
vestibular disorder			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
Eye disorders			
asthenopia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
cataract			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	3 / 276 (1.09%)	
occurrences (all)	1	3	
conjunctival haemorrhage			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
conjunctival hyperaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
conjunctivitis allergic		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
diabetic retinopathy		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
disorder of orbit		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
dry eye		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	2
entropion		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
eye disorder		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
eye irritation		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1

eye pruritus		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	2 / 276 (0.72%)
occurrences (all)	2	2
eye swelling		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
eyelid oedema		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
foreign body sensation in eyes		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
hypermetropia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
ocular hyperaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
ocular icterus		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)
occurrences (all)	2	1
periorbital oedema		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
photophobia		
alternative dictionary used: MedDRA 16.1		

subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences (all)	1	1	
presbyopia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
retinal vascular disorder			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
retinopathy			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
visual impairment			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
vision blurred			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 277 (1.44%)	3 / 276 (1.09%)	
occurrences (all)	4	3	
vitreous floaters			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	2 / 276 (0.72%)	
occurrences (all)	2	2	
Gastrointestinal disorders			
abdominal discomfort			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	7 / 276 (2.54%)	
occurrences (all)	2	8	
abdominal distension			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	19 / 277 (6.86%)	28 / 276 (10.14%)
occurrences (all)	27	31
abdominal hernia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
abdominal pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	45 / 277 (16.25%)	58 / 276 (21.01%)
occurrences (all)	63	86
abdominal pain lower		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	2
abdominal pain upper		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	26 / 277 (9.39%)	25 / 276 (9.06%)
occurrences (all)	34	32
abdominal rigidity		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
abdominal tenderness		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	2 / 276 (0.72%)
occurrences (all)	2	2
anal fissure		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
anal haemorrhage		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1

anal pruritus		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
aphthous stomatitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
ascites		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	72 / 277 (25.99%)	40 / 276 (14.49%)
occurrences (all)	110	47
breath odour		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
colitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	3	0
constipation		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	36 / 277 (13.00%)	34 / 276 (12.32%)
occurrences (all)	39	39
dental caries		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)
occurrences (all)	2	1
diarrhoea		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	50 / 277 (18.05%)	38 / 276 (13.77%)
occurrences (all)	74	52
dry mouth		
alternative dictionary used: MedDRA 16.1		

subjects affected / exposed	6 / 277 (2.17%)	4 / 276 (1.45%)
occurrences (all)	7	4
duodenal ulcer		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
dyspepsia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	6 / 277 (2.17%)	11 / 276 (3.99%)
occurrences (all)	7	14
dysphagia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	4 / 277 (1.44%)	2 / 276 (0.72%)
occurrences (all)	4	3
enteritis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	2
epigastric discomfort		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	3 / 276 (1.09%)
occurrences (all)	2	3
eructation		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
faecal incontinence		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
faeces discoloured		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	2	0

flatulence			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 277 (1.44%)	6 / 276 (2.17%)	
occurrences (all)	4	7	
food poisoning			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
frequent bowel movements			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
gastric mucosal lesion			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
gastric ulcer			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	2 / 276 (0.72%)	
occurrences (all)	2	2	
gastritis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	5 / 277 (1.81%)	5 / 276 (1.81%)	
occurrences (all)	6	5	
gastroduodenitis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
gastrointestinal disorder			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
gastrointestinal pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
gastrooesophageal reflux disease		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	5 / 277 (1.81%)	4 / 276 (1.45%)
occurrences (all)	6	4
gingival bleeding		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	18 / 277 (6.50%)	4 / 276 (1.45%)
occurrences (all)	22	4
gingival disorder		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
gingival pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	3	0
gingival swelling		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
glossodynia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
haematemesis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	2

haematochezia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)	
occurrences (all)	2	1	
haemorrhoidal haemorrhage			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	5 / 277 (1.81%)	1 / 276 (0.36%)	
occurrences (all)	6	1	
haemorrhoids			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	6 / 277 (2.17%)	4 / 276 (1.45%)	
occurrences (all)	6	4	
inguinal hernia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)	
occurrences (all)	3	1	
irritable bowel syndrome			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
lip dry			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)	
occurrences (all)	0	1	
lower gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences (all)	1	1	
melaena			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	3 / 276 (1.09%)	
occurrences (all)	2	3	
mouth ulceration			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	3 / 277 (1.08%)	3 / 276 (1.09%)
occurrences (all)	3	3
mouth haemorrhage		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	6 / 277 (2.17%)	0 / 276 (0.00%)
occurrences (all)	20	0
nausea		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	52 / 277 (18.77%)	52 / 276 (18.84%)
occurrences (all)	71	74
odynophagia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
oesophageal varices haemorrhage		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	3
oesophagitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	2 / 276 (0.72%)
occurrences (all)	2	3
oral disorder		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
oral mucosal blistering		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
painful defaecation		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0

paraesthesia oral		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
peptic ulcer		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
periodontal disease		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	4	0
portal hypertensive gastropathy		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
proctalgia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
rectal haemorrhage		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	5 / 277 (1.81%)	3 / 276 (1.09%)
occurrences (all)	5	3
rectal tenesmus		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
small intestinal obstruction		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
steatorrhoea		
alternative dictionary used: MedDRA 16.1		

subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
stomatitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	8 / 277 (2.89%)	4 / 276 (1.45%)
occurrences (all)	9	4
submaxillary gland enlargement		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
tongue geographic		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
tooth disorder		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
toothache		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	5 / 277 (1.81%)	2 / 276 (0.72%)
occurrences (all)	7	2
umbilical hernia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
upper gastrointestinal haemorrhage		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
varices oesophageal		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	2 / 276 (0.72%)
occurrences (all)	3	2

vomiting alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	30 / 277 (10.83%) 39	40 / 276 (14.49%) 47	
Hepatobiliary disorders			
biliary colic alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	1 / 276 (0.36%) 1	
cholangitis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	4 / 277 (1.44%) 6	0 / 276 (0.00%) 0	
cholangitis acute alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	0 / 277 (0.00%) 0	1 / 276 (0.36%) 3	
cholecystitis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
cholelithiasis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 4	0 / 276 (0.00%) 0	
cholestasis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
hepatic cirrhosis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	2 / 277 (0.72%) 2	1 / 276 (0.36%) 1	
hepatic failure alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	2 / 277 (0.72%)	5 / 276 (1.81%)
occurrences (all)	2	5
hepatic function abnormal		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	1 / 276 (0.36%)
occurrences (all)	3	1
hepatic pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	2 / 276 (0.72%)
occurrences (all)	3	3
hepatobiliary disease		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
hepatocellular injury		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
hepatorenal syndrome		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	2
hepatomegaly		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	6 / 277 (2.17%)	8 / 276 (2.90%)
occurrences (all)	6	8
hyperbilirubinaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	10 / 277 (3.61%)	15 / 276 (5.43%)
occurrences (all)	16	32
hypertransaminaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	1 / 276 (0.36%)
occurrences (all)	4	1

jaundice alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	12 / 277 (4.33%) 13	13 / 276 (4.71%) 14	
liver disorder alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
portal hypertension alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	1 / 276 (0.36%) 1	
portal vein thrombosis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	0 / 277 (0.00%) 0	4 / 276 (1.45%) 4	
Skin and subcutaneous tissue disorders			
acne alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	0 / 277 (0.00%) 0	3 / 276 (1.09%) 3	
alopecia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	12 / 277 (4.33%) 13	12 / 276 (4.35%) 13	
asteatosis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
blister alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
blood blister alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
cold sweat		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
cutis laxa		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
decubitus ulcer		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	2	0
dermatitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
dermatitis acneiform		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	5 / 277 (1.81%)	2 / 276 (0.72%)
occurrences (all)	5	3
dermatitis bullous		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
dermatitis contact		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
dermatitis diaper		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1

dry skin		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	16 / 277 (5.78%)	12 / 276 (4.35%)
occurrences (all)	17	13
ecchymosis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
eczema		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)
occurrences (all)	2	1
erythema		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	4 / 277 (1.44%)	6 / 276 (2.17%)
occurrences (all)	5	6
haemorrhage subcutaneous		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
hair colour changes		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
hand dermatitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
hyperhidrosis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	5 / 276 (1.81%)
occurrences (all)	1	5
hyperkeratosis		
alternative dictionary used: MedDRA 16.1		

subjects affected / exposed	1 / 277 (0.36%)	3 / 276 (1.09%)
occurrences (all)	1	3
koilonychia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
leukocytoclastic vasculitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
lichenoid keratosis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
nail disorder		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	2	0
nail dystrophy		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
night sweats		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
onychoclasia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)
occurrences (all)	2	1
onychomadesis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0

palmar-plantar erythrodysaesthesia syndrome		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	11 / 277 (3.97%)	5 / 276 (1.81%)
occurrences (all)	19	5
papule		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
petechiae		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	2	0
photodermatitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
photosensitivity reaction		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
pigmentation disorder		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	2	0
prurigo		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
pruritus		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	28 / 277 (10.11%)	29 / 276 (10.51%)
occurrences (all)	33	41
pruritus generalised		
alternative dictionary used: MedDRA 16.1		

subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
purpura		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)
occurrences (all)	2	1
purpura senile		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
rash		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	23 / 277 (8.30%)	12 / 276 (4.35%)
occurrences (all)	27	16
rash erythematous		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
rash maculo-papular		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	1 / 276 (0.36%)
occurrences (all)	3	1
scar pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
skin atrophy		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
skin disorder		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1

skin exfoliation		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
skin haemorrhage		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
skin hyperpigmentation		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	2	0
skin hypopigmentation		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
skin lesion		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	1 / 276 (0.36%)
occurrences (all)	3	1
skin mass		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	0 / 276 (0.00%)
occurrences (all)	3	0
skin tightness		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
skin ulcer		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	2 / 276 (0.72%)
occurrences (all)	5	2
swelling face		
alternative dictionary used: MedDRA 16.1		

<p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 277 (0.36%)</p> <p>1</p>	<p>0 / 276 (0.00%)</p> <p>0</p>	
<p>urticaria</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 277 (0.36%)</p> <p>1</p>	<p>2 / 276 (0.72%)</p> <p>3</p>	
<p>xeroderma</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 277 (0.00%)</p> <p>0</p>	<p>1 / 276 (0.36%)</p> <p>1</p>	
Renal and urinary disorders			
<p>anuria</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 277 (0.36%)</p> <p>1</p>	<p>0 / 276 (0.00%)</p> <p>0</p>	
<p>dysuria</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 277 (0.72%)</p> <p>2</p>	<p>1 / 276 (0.36%)</p> <p>1</p>	
<p>haematuria</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 277 (0.36%)</p> <p>1</p>	<p>3 / 276 (1.09%)</p> <p>3</p>	
<p>nephropathy</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 277 (0.36%)</p> <p>1</p>	<p>0 / 276 (0.00%)</p> <p>0</p>	
<p>nocturia</p> <p>alternative dictionary used: MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 277 (0.72%)</p> <p>2</p>	<p>1 / 276 (0.36%)</p> <p>2</p>	
<p>oliguria</p> <p>alternative dictionary used: MedDRA 16.1</p>			

subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	2	0
pollakiuria		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	4 / 277 (1.44%)	1 / 276 (0.36%)
occurrences (all)	4	1
polyuria		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
proteinuria		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	46 / 277 (16.61%)	13 / 276 (4.71%)
occurrences (all)	117	18
renal cyst		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
renal failure		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	2 / 276 (0.72%)
occurrences (all)	2	2
renal failure acute		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	3 / 276 (1.09%)
occurrences (all)	2	3
renal impairment		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
renal pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1

renal vein thrombosis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	0 / 277 (0.00%) 0	1 / 276 (0.36%) 1	
urinary incontinence alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	2 / 277 (0.72%) 3	1 / 276 (0.36%) 1	
urinary retention alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	2 / 277 (0.72%) 3	1 / 276 (0.36%) 1	
Endocrine disorders adrenal insufficiency alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
hyperparathyroidism alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
hyperthyroidism alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
hypothyroidism alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	3 / 277 (1.08%) 3	0 / 276 (0.00%) 0	
Musculoskeletal and connective tissue disorders amyotrophy alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	1 / 276 (0.36%) 1	
arthralgia			

alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	19 / 277 (6.86%)	10 / 276 (3.62%)
occurrences (all)	26	12
arthritis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	2	0
back pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	23 / 277 (8.30%)	23 / 276 (8.33%)
occurrences (all)	27	32
bone pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	5 / 277 (1.81%)	4 / 276 (1.45%)
occurrences (all)	20	4
bursitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
exostosis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
flank pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	11 / 276 (3.99%)
occurrences (all)	3	16
groin pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
intervertebral disc protrusion		
alternative dictionary used: MedDRA 16.1		

subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)
occurrences (all)	2	1
joint crepitation		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
joint effusion		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
joint stiffness		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
joint swelling		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	4
lumbar spinal stenosis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
metatarsalgia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
mobility decreased		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
muscle atrophy		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1

muscle spasms		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	6 / 277 (2.17%)	6 / 276 (2.17%)
occurrences (all)	11	7
muscular weakness		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	5 / 277 (1.81%)	4 / 276 (1.45%)
occurrences (all)	6	4
musculoskeletal chest pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	7 / 277 (2.53%)	11 / 276 (3.99%)
occurrences (all)	9	13
musculoskeletal pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	18 / 277 (6.50%)	12 / 276 (4.35%)
occurrences (all)	26	13
musculoskeletal stiffness		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
myalgia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	11 / 277 (3.97%)	7 / 276 (2.54%)
occurrences (all)	14	9
neck mass		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
neck pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	2 / 276 (0.72%)
occurrences (all)	2	2
osteoarthritis		
alternative dictionary used: MedDRA 16.1		

subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
osteonecrosis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
pain in extremity		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	12 / 277 (4.33%)	6 / 276 (2.17%)
occurrences (all)	14	8
pain in jaw		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	2	0
pathological fracture		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	2	0
rheumatic disorder		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
scleroderma		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
spinal osteoarthritis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
spinal pain		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	4 / 276 (1.45%)
occurrences (all)	0	4

temporomandibular joint syndrome alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
tenosynovitis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 277 (0.36%) 1	0 / 276 (0.00%) 0	
Infections and infestations			
abdominal infection alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	0 / 277 (0.00%) 0	1 / 276 (0.36%) 1	
anal abscess alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	2 / 277 (0.72%) 2	0 / 276 (0.00%) 0	
anisakiasis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	0 / 277 (0.00%) 0	1 / 276 (0.36%) 1	
biliary tract infection alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	0 / 277 (0.00%) 0	1 / 276 (0.36%) 1	
bronchitis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	5 / 277 (1.81%) 5	3 / 276 (1.09%) 3	
bronchopneumonia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	2 / 277 (0.72%) 2	0 / 276 (0.00%) 0	
candida infection alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	2
cellulitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
cystitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
diarrhoea infectious		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
ear infection		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
erysipelas		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
fungus infection		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
gastroenteritis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	0 / 276 (0.00%)
occurrences (all)	3	0
gastroenteritis bacterial		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1

gingival abscess		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
gingivitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	4 / 277 (1.44%)	0 / 276 (0.00%)
occurrences (all)	6	0
hepatitis a		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
herpes simplex		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	2
herpes zoster		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
infection		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	3 / 276 (1.09%)
occurrences (all)	1	3
influenza		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)
occurrences (all)	2	1
kidney infection		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
labyrinthitis		
alternative dictionary used: MedDRA 16.1		

subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
laryngitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	2	0
lip infection		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
liver abscess		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
localised infection		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
lung infection		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
nasopharyngitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	15 / 277 (5.42%)	14 / 276 (5.07%)
occurrences (all)	15	16
oesophageal candidiasis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
oral candidiasis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1

oral herpes		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	3 / 276 (1.09%)
occurrences (all)	1	3
oral infection		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
paronychia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
periodontitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
peritonitis bacterial		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
pharyngitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
pharyngotonsillitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
pneumonia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	2
proteus infection		
alternative dictionary used: MedDRA 16.1		

subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
pyelonephritis acute		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
rash pustular		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	0 / 276 (0.00%)
occurrences (all)	3	0
respiratory tract infection		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	3 / 277 (1.08%)	1 / 276 (0.36%)
occurrences (all)	3	1
rhinitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	6 / 277 (2.17%)	0 / 276 (0.00%)
occurrences (all)	7	0
sepsis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
sinusitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	4 / 277 (1.44%)	1 / 276 (0.36%)
occurrences (all)	4	1
skin candida		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
staphylococcal infection		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0

tinea cruris		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
tinea pedis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)
occurrences (all)	2	1
tinea infection		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
tonsillitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
tooth abscess		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	1 / 276 (0.36%)
occurrences (all)	2	1
tooth infection		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
tracheitis		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
upper respiratory tract infection		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	11 / 277 (3.97%)	6 / 276 (2.17%)
occurrences (all)	14	8
urinary tract infection		
alternative dictionary used: MedDRA 16.1		

subjects affected / exposed	10 / 277 (3.61%)	6 / 276 (2.17%)	
occurrences (all)	10	6	
urinary tract infection bacterial			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	1	0	
vulvovaginal candidiasis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed ^[6]	0 / 47 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	2	
vulvitis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed ^[7]	1 / 47 (2.13%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
cachexia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)	
occurrences (all)	1	1	
decreased appetite			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	59 / 277 (21.30%)	50 / 276 (18.12%)	
occurrences (all)	81	62	
dehydration			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	8 / 277 (2.89%)	5 / 276 (1.81%)	
occurrences (all)	9	5	
diabetes mellitus			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 277 (0.72%)	4 / 276 (1.45%)	
occurrences (all)	2	4	
fluid retention			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	2	0
glucose tolerance impaired		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	2	0
gout		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
hyperammonaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	2 / 276 (0.72%)
occurrences (all)	1	2
hypercalcaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	3 / 276 (1.09%)
occurrences (all)	2	4
hypercreatininaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	3	0
hyperglycaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	9 / 277 (3.25%)	11 / 276 (3.99%)
occurrences (all)	26	15
hyperkalaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	13 / 277 (4.69%)	11 / 276 (3.99%)
occurrences (all)	17	11
hypernatraemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0

hyperphagia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
hypertriglyceridaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	3	0
hyperuricaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	8 / 277 (2.89%)	4 / 276 (1.45%)
occurrences (all)	20	5
hypoalbuminaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	33 / 277 (11.91%)	14 / 276 (5.07%)
occurrences (all)	66	27
hypocalcaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	4 / 277 (1.44%)	3 / 276 (1.09%)
occurrences (all)	11	3
hypoglycaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
hypokalaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	7 / 277 (2.53%)	10 / 276 (3.62%)
occurrences (all)	9	15
hypomagnesaemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	4 / 277 (1.44%)	3 / 276 (1.09%)
occurrences (all)	5	3
hyponatraemia		
alternative dictionary used: MedDRA 16.1		

subjects affected / exposed	13 / 277 (4.69%)	15 / 276 (5.43%)
occurrences (all)	21	20
hypophosphataemia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	5 / 277 (1.81%)	3 / 276 (1.09%)
occurrences (all)	9	6
increased appetite		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	2 / 277 (0.72%)	0 / 276 (0.00%)
occurrences (all)	2	0
iron deficiency		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	1 / 276 (0.36%)
occurrences (all)	1	1
malnutrition		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	2 / 276 (0.72%)
occurrences (all)	0	2
polydipsia		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
type 2 diabetes mellitus		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	0 / 277 (0.00%)	1 / 276 (0.36%)
occurrences (all)	0	1
vitamin b1 deficiency		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0
vitamin b6 deficiency		
alternative dictionary used: MedDRA 16.1		
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)
occurrences (all)	1	0

vitamin d deficiency			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 277 (0.36%)	0 / 276 (0.00%)	
occurrences (all)	2	0	

Notes:

[1] - 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.

[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.

[6] - 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.

[7] - 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? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported