Clinical trial results:
FAST- Febuxostat versus Allopurinol Streamlined Trial A prospective, randomised, open-label, blinded endpoint (PROBE) clinical trial evaluating long term cardiovascular safety of febuxostat in comparison with allopurinol in patients with chronic symptomatic hyperuricaemia

Summary

EudraCT number	2011-001883-23
Trial protocol	GB DK FI SE
Global end of trial date	31 August 2020

Results information

Result version number	v1 (current)
This version publication date	05 May 2021
First version publication date	05 May 2021

Trial information

Trial identification

Sponsor protocol code	2011CV08 (FAST)

Additional study identifiers

ISRCTN number	ISRCTN72443728
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Dundee
Sponsor organisation address	Ninewells Hospital & Medical School, Dundee, United Kingdom,
Public contact	Professor Tom MacDonald, MEMO Research, University of Dundee, +44 1382383119, t.m.macdonald@dundee.ac.uk
Scientific contact	Professor Tom MacDonald, MEMO Research, University of Dundee, +44 1382383119, t.m.macdonald@dundee.ac.uk

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	28 January 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 January 2020
Global end of trial reached?	Yes
Global end of trial date	31 August 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to compare the cardiovascular safety profile of febuxostat versus allopurinol when taken for an average of 3 years in patients over 60 years with chronic hyperuricaemia in conditions where urate deposition has already occurred

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki, Good Clinical Practice (GCP) guidelines and local law requirements.

Background therapy:

Treatment of acute gout flares was allowed according to clinical judgement, e.g. with non-steroidal anti-inflammatory drugs (NSAIDs), colchicine, corticosteroids.

Evidence for comparator: -

Actual start date of recruitment	20 December 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 2099
Country: Number of subjects enrolled	Sweden: 140
Country: Number of subjects enrolled	United Kingdom: 4364
Worldwide total number of subjects	6603
EEA total number of subjects	2239

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)	1324
From 65 to 84 years	5095
85 years and over	184

Subject disposition

Recruitment

Recruitment details:

Screening period from 20 December 2011 to 17 October 2017. A total of 7552 subjects were screened and 6603 consented to enroll from the UK, Denmark and Sweden. Patients were included with gout, aged over 60 years, with at least 1 additional CV risk factor and already treated with allopurinol.

Pre-assignment

Screening details:

Age was missing for 3/6603 enrolled patients (these patients are included as 65-85 in the by age summary). Of the 6603 consented patients, 6435 were eligible and either entered the lead-in phase (urate at least 6 mg/dL) or continued directly to randomization (urate below 6 mg/dL). Washout period of 1 week.

Pre-assignment period milestones

Number of subjects started	6603
Number of subjects completed	6128

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Ineligible: 168
Reason: Number of subjects	Withdrew prior to randomisation: 307

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

The primary endpoint was blinded. Cardiovascular events were adjudicated by an independent committee that was blinded to randomisation and subsequent treatment groups. Recruitment and blinded accumulation of study endpoints were reviewed by the study steering committee on an ongoing basis. The pharmacovigilance group reviewed blinded SAEs.

Arms

Are arms mutually exclusive?	Yes
Arm title	Febuxostat

Arm description:

All patients randomised to febuxostat treatment received 80 mg initially and sUA level was determined after 2 weeks of treatment (range 9 to 24 days). Patients with a sUA level of ≥6 mg/dL had their dose increased to febuxostat 120 mg daily, followed by the determination of their sUA level 2 weeks later. Patients then continued to receive treatment according to clinical judgement, EULAR recommendations and the current SmPC.

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

Dosage and administration details:

All patients randomised to febuxostat treatment received 80 mg initially and sUA level was determined after 2 weeks of treatment (range 9 to 24 days). Patients with a sUA level of ≥6 mg/dL had their dose increased to febuxostat 120 mg daily, followed by the determination of their sUA level 2 weeks later. Patients then continued to receive treatment according to clinical judgement, EULAR recommendations

and the current SmPC.

Arm title	Allopurinol

Arm description:

In accordance with the current SmPC, allopurinol dosing could be in the range of 100 to 900 mg per day. Patients randomised to allopurinol received allopurinol at the dose determined before randomisation. During the course of the study, the dose was adjusted according to clinical judgement as determined by EULAR recommendations and the current SmPC.

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

Dosage and administration details:

In accordance with the current SmPC, allopurinol dosing could be in the range of 100 to 900 mg per day. Patients randomised to allopurinol received allopurinol at the dose determined before randomisation. During the course of the study, the dose was adjusted according to clinical judgement as determined by EULAR recommendations and the current SmPC.

Number of subjects in period 1[1]	Febuxostat	Allopurinol
Started	3063	3065
Completed	2652	2633
Not completed	411	432
Physician decision	20	17
Consent withdrawn by subject	107	98
died	222	263
moved from study area	15	26
Adverse event	28	11
other	-	1
Serious adverse event	12	9
Lost to follow-up	2	1
Protocol deviation	5	6

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Only 6128 randomized patients are included in the "overall trial" and therefore the baseline period.

Baseline characteristics

Reporting groups	
Reporting group title	Febuxostat

Reporting group description:

All patients randomised to febuxostat treatment received 80 mg initially and sUA level was determined after 2 weeks of treatment (range 9 to 24 days). Patients with a sUA level of ≥6 mg/dL had their dose increased to febuxostat 120 mg daily, followed by the determination of their sUA level 2 weeks later. Patients then continued to receive treatment according to clinical judgement, EULAR recommendations and the current SmPC.

Reporting group title	Allopurinol

Reporting group description:

In accordance with the current SmPC, allopurinol dosing could be in the range of 100 to 900 mg per day. Patients randomised to allopurinol received allopurinol at the dose determined before randomisation. During the course of the study, the dose was adjusted according to clinical judgement as determined by EULAR recommendations and the current SmPC.

Reporting group values	Febuxostat	Allopurinol	Total
Number of subjects	3063	3065	6128
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	70.99	70.90	
standard deviation	± 6.37	± 6.50	-
Gender categorical Units: Subjects			
Female	444	459	903
Male	2619	2606	5225
Race Units: Subjects			
White	3034	3036	6070
Asian	11	14	25
Afro-Carribbean	10	8	18
Oriental	2	1	3
Other	6	6	12
Allopurinol dose up-titrated during lead-in Units: Subjects			
Yes	1104	1097	2201
No	1959	1968	3927

Duration of allopurinol treatment			
At time of screening			
Units: years			
arithmetic mean	9.35	9.48	
standard deviation	± 9.28	± 9.31	-

End points

End points reporting groups

Reporting group title	Febuxostat

Reporting group description:

All patients randomised to febuxostat treatment received 80 mg initially and sUA level was determined after 2 weeks of treatment (range 9 to 24 days). Patients with a sUA level of ≥6 mg/dL had their dose increased to febuxostat 120 mg daily, followed by the determination of their sUA level 2 weeks later. Patients then continued to receive treatment according to clinical judgement, EULAR recommendations and the current SmPC.

Reporting group title	Allopurinol

Reporting group description:

In accordance with the current SmPC, allopurinol dosing could be in the range of 100 to 900 mg per day. Patients randomised to allopurinol received allopurinol at the dose determined before randomisation. During the course of the study, the dose was adjusted according to clinical judgement as determined by EULAR recommendations and the current SmPC.

Primary: Primary outcome (on-treatment)

End point title	Primary outcome (on-treatment)

End point description:

The Anti-Platelet Trialists' Collaboration primary composite endpoint included hospitalisation for non-fatal MI/biomarker positive ACS, non-fatal stroke [whether reported to have been hospitalised, non-hospitalised or to have occurred during a hospitalisation] or death due to a CV event.

End point type	Primary

End point timeframe:

Time from randomization to first occurrence of a primary endpoint event.

End point values	Febuxostat	Allopurinol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3063	3065		
Units: subjects				
Primary endpoint	172	241		

Attachments (see zip file)	Primary on-treatment analysis/FAST_FIGURE2a_PRIM_OT.pdf

Statistical analyses

Statistical analysis title	On-treatment analysis

Statistical analysis description:

The OT analysis censored patients after permanent discontinuation from original randomised therapy, death from any cause not included in the endpoint being considered, date of withdrawal of all consent to participate further in the study, date of loss to follow-up or end of study, whichever occurred first.

Comparison groups	Febuxostat v Allopurinol

Number of subjects included in analysis	6128
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.001 [2]
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.03

Notes:

[1] - Non-inferiority was to be claimed if the upper limit of the 95% CI for the HR was ≤1.3.

[2] - The hazard ratio (febuxostat versus allopurinol) in a Cox proportional hazards model was assessed for
non-inferiority (limit of 1·3). All analyses were adjusted for the stratification variable and country. P-value was calculated from Wald statistic

Primary: Primary outcome (intent-to-treat)

End point title	Primary outcome (intent-to-treat)

End point description:

The Anti-Platelet Trialist' Collaboration primary composite endpoint included hospitalisation for non-fatal MI/biomarker positive ACS, non-fatal stroke [whether reported to have been hospitalised, non-hospitalised or to have occurred during a hospitalisation] or death due to a CV event.

End point type	Primary

End point timeframe:

Time from randomization to first occurrence of a primary endpoint event

End point values	Febuxostat	Allopurinol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3063	3065		
Units: subjects				
Primary event	256	285		

Attachments (see zip file)	FAST_FIGURE2a_PRIM_OT.pdf

Statistical analyses

Statistical analysis title	Intent-to-treat analysis

Statistical analysis description:

The ITT analysis censored patients after death from any cause not included in the endpoint being considered, date of withdrawal of all consent to participate further in the study, date of loss to follow-up or end of study, whichever occurred first.

Comparison groups	Febuxostat v Allopurinol

Number of subjects included in analysis	6128
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.185 [4]
Method	Cox proportional hazards model
Parameter estimate	Cox proportional hazard
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.06

Notes:

[3] - If non-inferiority was demonstrated, a superiority analysis was carried out based on ITT.

[4] - The type I error rate was set at 5% for 2-sided superiority analyses. P-value was calculated from Wald statistics. Superiority of febuxostat for the primary outcome was not demonstrated.

Statistical analysis title	Intent-to-treat analysis

Statistical analysis description:

The ITT analysis censored patients after death from any cause not included in the endpoint being considered, date of withdrawal of all consent to participate further in the study, date of loss to follow-up or end of study, whichever occurred first.

Comparison groups	Febuxostat v Allopurinol
Number of subjects included in analysis	6128
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
P-value	< 0.001 [6]
Method	Cox proportional hazards model
Parameter estimate	Cox proportional hazard
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.06

Notes:

[5] - The first analysis to be carried out was a non-inferiority analysis of the primary outcome based on an OT analysis (covering the period patients remain on randomized therapy), with a supporting non-inferiority analysis using an ITT analysis.

[6] - The ITT analysis of the primary endpoint confirmed non-inferiority of febuxostat

Secondary: Secondary - hospitalisation for non-fatal MI/ACS (on-treatment)

End point title	Secondary - hospitalisation for non-fatal MI/ACS (on-treatment)

End point description:

Secondary endpoint event of hospitalisation for non-fatal myocardial infarction/ biomarker positive acute coronary syndrome

End point type	Secondary

End point timeframe:

Time from randomization to first occurrence of the secondary endpoint event

End point values	Febuxostat	Allopurinol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3063	3065		
Units: subjects				
Hospitilsation for non-fatal MI/ACS	77	98		

Statistical analyses

Statistical analysis title	On-treatment analysis
Comparison groups	Febuxostat v Allopurinol
Number of subjects included in analysis	6128
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.016
Method	Cox proportional hazards model
Parameter estimate	Cox proportional hazard
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.27

Secondary: Secondary - non-fatal stroke (on-treatment)

End point title	Secondary - non-fatal stroke (on-treatment)
End point description:	
Secondary endpoint of non-fatal stroke	
End point type	Secondary
End point timeframe:	
Time from randomization to first occurrence of the secondary endpoint event	

End point values	Febuxostat	Allopurinol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3063	3065		
Units: subjects				
Secondary event	58	80		

Statistical analyses

Statistical analysis title	On-treatment analysis
Comparison groups	Febuxostat v Allopurinol

Number of subjects included in analysis	6128
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.009
Method	Cox proportional hazards model
Parameter estimate	Cox proportional hazard
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.21

Secondary: Secondary - cardiovascular death (on-treatment)	
End point title	Secondary - cardiovascular death (on-treatment)
End point description:	
Secondary endpoint of cardiovascular death.	
End point type	Secondary
End point timeframe:	
Time from randomization to first occurrence of the secondary endpoint event	

End point values	Febuxostat	Allopurinol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3063	3065		
Units: subjects				
Secondary event	62	82		

Attachments (see zip file)	FAST_FIGURE3c_CVDEATH_OT.pdf

Statistical analyses

Statistical analysis title	On-treatment analysis
Comparison groups	Febuxostat v Allopurinol
Number of subjects included in analysis	6128
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.018
Method	Cox proportional hazards model
Parameter estimate	Cox proportional hazard
Point estimate	0.91

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.27

Secondary: Secondary - all-cause mortality (on-treatment)

End point title	Secondary - all-cause mortality (on-treatment)

End point description:

Secondary endpoint of all-cause mortality

End point type	Secondary

End point timeframe:

Time from randomization to first occurrence of the secondary endpoint event

End point values	Febuxostat	Allopurinol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3063	3065		
Units: subjects				
Secondary event	108	174		

Attachments (see zip file)	FAST_FIGURE3a_ACM_OT.pdf

Statistical analyses

Statistical analysis title	On-treatment analysis
Comparison groups	Febuxostat v Allopurinol
Number of subjects included in analysis	6128
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Cox proportional hazards model
Parameter estimate	Cox proportional hazard
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	0.95

Secondary: Secondary - hospitalisation for non-fatal MI/ACS (intent-to-treat)

End point title	Secondary - hospitalisation for non-fatal MI/ACS (intent-to-treat)

End point description:

Secondary endpoint of hospitalisation for non-fatal myocardial infarction/biomarker positive acute coronary syndrome

End point type	Secondary

End point timeframe:

Time from randomization to first occurrence of the secondary endpoint event

End point values	Febuxostat	Allopurinol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3063	3065		
Units: subjects				
Secondary event	102	110		

Statistical analyses

Statistical analysis title	Intent-to-treat analysis
Comparison groups	Febuxostat v Allopurinol
Number of subjects included in analysis	6128
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.007
Method	Cox proportional hazards model
Parameter estimate	Cox proportional hazard
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.21

Secondary: Secondary - non-fatal stroke (intent-to-treat)

End point title	Secondary - non-fatal stroke (intent-to-treat)

End point description:

Secondary endpoint of non-fatal stroke

End point type	Secondary

End point timeframe:

Time from randomization to first occurrence of the secondary endpoint event

End point values	Febuxostat	Allopurinol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3063	3065		
Units: subjects				
Secondary event	80	87		

Statistical analyses

Statistical analysis title	Intent-to-treat analysis
Comparison groups	Febuxostat v Allopurinol
Number of subjects included in analysis	6128
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.013
Method	Cox proportional hazards model
Parameter estimate	Cox proportional hazard
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.25

Secondary: Secondary - cardiovascular death (intent-to-treat)

End point title	Secondary - cardiovascular death (intent-to-treat)
End point description:	
Secondary endpoint of cardiovascular death	
End point type	Secondary
End point timeframe:	
Time from randomization to first occurrence of the secondary endpoint event	

End point values	Febuxostat	Allopurinol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3063	3065		
Units: subjects				
Secondary event	117	122		

Attachments (see zip file)	FAST_FIGURE3d_CVDEATH_ITT.pdf

Statistical analyses

Statistical analysis title	Intent-to-treat analysis
Comparison groups	Febuxostat v Allopurinol
Number of subjects included in analysis	6128
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.009
Method	Cox proportional hazards model
Parameter estimate	Cox proportional hazard
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.23

Secondary: Secondary - all-cause mortality (intent-to-treat)	
End point title	Secondary - all-cause mortality (intent-to-treat)
End point description:	
Secondary endpoint of all-cause mortality	
End point type	Secondary
End point timeframe:	
Time from randomization to first occurrence of the secondary endpoint event	

End point values	Febuxostat	Allopurinol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3063	3065		
Units: subjects				
Secondary event	222	263		

Attachments (see zip file)	FAST_FIGURE3b_ACM_ITT.pdf

Statistical analyses

Statistical analysis title	Intent-to-treat analysis
Comparison groups	Febuxostat v Allopurinol
Number of subjects included in analysis	6128
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Cox proportional hazards model
Parameter estimate	Cox proportional hazard
Point estimate	0.84

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.01

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Summaries of AEs are presented for during treatment (randomisation up to date of death or end of study IMP plus 28 days, whichever came first).

Adverse event reporting additional description:

SAEs (related or unrelated to study treatment) and AEs only considered related to treatment were recorded during the stud and collected separately. Related SAE data do not overlap with related AE data. "Occurrence" equals number of patients. Total of non-serious AEs equals summation of each AE term with incidence >1% and is not an overall total.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	Febuxostat (safety population) - during the treatment period

Reporting group description:

The safety population was defined as the randomized population, excluding those patients where there was clear evidence that no study drug was taken. During treatment is defined as randomization up to date of death or end of study IMP plus 28 days, whichever came first.

Reporting group title	Allopurinol (safety population) - during the treatment period

Reporting group description:

The safety population was defined as the randomised population, excluding those patients where there was clear evidence that no study drug was taken. During treatment is defined as randomisation up to date of death or end of study IMP plus 28 days, whichever came first.

Serious adverse events	Febuxostat (safety population) - during the treatment period	Allopurinol (safety population) - during the treatment period	
Total subjects affected by serious adverse events			
subjects affected / exposed	1527 / 3001 (50.88%)	1771 / 3050 (58.07%)	
number of deaths (all causes)	147	224	
number of deaths resulting from adverse events	147	224	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin cancer			
subjects affected / exposed	53 / 3001 (1.77%)	70 / 3050 (2.30%)	
occurrences causally related to treatment / all	0 / 53	0 / 70	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	47 / 3001 (1.57%)	65 / 3050 (2.13%)	
occurrences causally related to treatment / all	0 / 47	0 / 65	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung neoplasm malignant			

subjects affected / exposed	15 / 3001 (0.50%)	19 / 3050 (0.62%)	
occurrences causally related to treatment / all	0 / 15	0 / 19	
deaths causally related to treatment / all	0 / 4	0 / 5	
Pancreatic carcinoma			
subjects affected / exposed	9 / 3001 (0.30%)	8 / 3050 (0.26%)	
occurrences causally related to treatment / all	0 / 9	0 / 8	
deaths causally related to treatment / all	0 / 5	0 / 4	
Lung cancer metastatic			
subjects affected / exposed	5 / 3001 (0.17%)	5 / 3050 (0.16%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 2	0 / 5	
Brain neoplasm			
subjects affected / exposed	1 / 3001 (0.03%)	8 / 3050 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 5	
Neoplasm malignant			
subjects affected / exposed	5 / 3001 (0.17%)	7 / 3050 (0.23%)	
occurrences causally related to treatment / all	0 / 5	0 / 7	
deaths causally related to treatment / all	0 / 2	0 / 3	
Hepatic neoplasm malignant			
subjects affected / exposed	8 / 3001 (0.27%)	3 / 3050 (0.10%)	
occurrences causally related to treatment / all	0 / 8	0 / 3	
deaths causally related to treatment / all	0 / 2	0 / 2	
Bladder cancer			
subjects affected / exposed	11 / 3001 (0.37%)	14 / 3050 (0.46%)	
occurrences causally related to treatment / all	0 / 11	0 / 14	
deaths causally related to treatment / all	0 / 2	0 / 1	
Colon cancer			
subjects affected / exposed	12 / 3001 (0.40%)	19 / 3050 (0.62%)	
occurrences causally related to treatment / all	0 / 12	0 / 19	
deaths causally related to treatment / all	0 / 2	0 / 1	
Prostate cancer metastatic			

subjects affected / exposed	3 / 3001 (0.10%)	7 / 3050 (0.23%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 2	
Bile duct cancer			
subjects affected / exposed	2 / 3001 (0.07%)	6 / 3050 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 1	
Colon cancer metastatic			
subjects affected / exposed	1 / 3001 (0.03%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Colorectal cancer			
subjects affected / exposed	3 / 3001 (0.10%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 0	
Glioblastoma			
subjects affected / exposed	1 / 3001 (0.03%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Lung adenocarcinoma			
subjects affected / exposed	2 / 3001 (0.07%)	3 / 3050 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Lung adenocarcinoma metastatic			
subjects affected / exposed	2 / 3001 (0.07%)	0 / 3050 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Malignant melanoma			
subjects affected / exposed	3 / 3001 (0.10%)	16 / 3050 (0.52%)	
occurrences causally related to treatment / all	0 / 3	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 2	
Metastases to central nervous system			

subjects affected / exposed	1 / 3001 (0.03%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Metastatic malignant melanoma			
subjects affected / exposed	1 / 3001 (0.03%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Oesophageal carcinoma			
subjects affected / exposed	5 / 3001 (0.17%)	6 / 3050 (0.20%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 2	0 / 0	
Renal cancer			
subjects affected / exposed	6 / 3001 (0.20%)	8 / 3050 (0.26%)	
occurrences causally related to treatment / all	0 / 6	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 1	
Acute myeloid leukaemia			
subjects affected / exposed	1 / 3001 (0.03%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bone sarcoma			
subjects affected / exposed	1 / 3001 (0.03%)	0 / 3050 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Endometrial cancer			
subjects affected / exposed	0 / 3001 (0.00%)	4 / 3050 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastric cancer			
subjects affected / exposed	2 / 3001 (0.07%)	3 / 3050 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Leukaemia			

subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Leukaemia plasmacytic			
subjects affected / exposed	1 / 3001 (0.03%)	0 / 3050 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lymphoma			
subjects affected / exposed	2 / 3001 (0.07%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant neoplasm of renal pelvis			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Mantle cell lymphoma			
subjects affected / exposed	1 / 3001 (0.03%)	0 / 3050 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Mesothelioma			
subjects affected / exposed	1 / 3001 (0.03%)	0 / 3050 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastases to abdominal cavity			
subjects affected / exposed	1 / 3001 (0.03%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to liver			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to lung			

subjects affected / exposed	1 / 3001 (0.03%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastatic carcinoma of the bladder			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastatic gastric cancer			
subjects affected / exposed	1 / 3001 (0.03%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastatic neoplasm			
subjects affected / exposed	0 / 3001 (0.00%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myelodysplastic syndrome			
subjects affected / exposed	1 / 3001 (0.03%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Non-Hodgkin's lymphoma			
subjects affected / exposed	5 / 3001 (0.17%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Non-small cell lung cancer			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Non-small cell lung cancer stage IV			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oesophageal adenocarcinoma			

subjects affected / exposed	1 / 3001 (0.03%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oesophageal squamous cell carcinoma			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ovarian cancer			
subjects affected / exposed	0 / 3001 (0.00%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pancreatic carcinoma metastatic			
subjects affected / exposed	1 / 3001 (0.03%)	0 / 3050 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Rectal cancer			
subjects affected / exposed	10 / 3001 (0.33%)	8 / 3050 (0.26%)	
occurrences causally related to treatment / all	0 / 10	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal cancer metastatic			
subjects affected / exposed	0 / 3001 (0.00%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sarcoma			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Small intestine carcinoma metastatic			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ureteric cancer metastatic			

subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Uterine cancer			
subjects affected / exposed	2 / 3001 (0.07%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Aortic aneurysm rupture			
subjects affected / exposed	3 / 3001 (0.10%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 3	0 / 2	
Aortic aneurysm			
subjects affected / exposed	10 / 3001 (0.33%)	11 / 3050 (0.36%)	
occurrences causally related to treatment / all	0 / 10	0 / 11	
deaths causally related to treatment / all	0 / 1	0 / 1	
Aortic stenosis			
subjects affected / exposed	11 / 3001 (0.37%)	13 / 3050 (0.43%)	
occurrences causally related to treatment / all	0 / 11	0 / 13	
deaths causally related to treatment / all	0 / 1	0 / 1	
Circulatory collapse			
subjects affected / exposed	20 / 3001 (0.67%)	27 / 3050 (0.89%)	
occurrences causally related to treatment / all	1 / 20	0 / 27	
deaths causally related to treatment / all	1 / 1	0 / 1	
Deep vein thrombosis			
subjects affected / exposed	11 / 3001 (0.37%)	20 / 3050 (0.66%)	
occurrences causally related to treatment / all	0 / 11	0 / 20	
deaths causally related to treatment / all	0 / 1	0 / 1	
Aneurysm ruptured			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arteriosclerosis			

subjects affected / exposed	12 / 3001 (0.40%)	26 / 3050 (0.85%)	
occurrences causally related to treatment / all	0 / 12	0 / 26	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vasculitis			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Surgical and medical procedures			
Hip arthroplasty			
subjects affected / exposed	23 / 3001 (0.77%)	41 / 3050 (1.34%)	
occurrences causally related to treatment / all	0 / 23	0 / 41	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee arthroplasty			
subjects affected / exposed	25 / 3001 (0.83%)	34 / 3050 (1.11%)	
occurrences causally related to treatment / all	0 / 25	0 / 34	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endarterectomy			
subjects affected / exposed	1 / 3001 (0.03%)	0 / 3050 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pacemaker generated rhythm			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Palliative care			
subjects affected / exposed	2 / 3001 (0.07%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Proctocolectomy			
subjects affected / exposed	1 / 3001 (0.03%)	0 / 3050 (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			

Chest pain			
subjects affected / exposed	52 / 3001 (1.73%)	87 / 3050 (2.85%)	
occurrences causally related to treatment / all	0 / 52	0 / 87	
deaths causally related to treatment / all	0 / 0	0 / 1	
Death			
subjects affected / exposed	14 / 3001 (0.47%)	19 / 3050 (0.62%)	
occurrences causally related to treatment / all	0 / 14	0 / 19	
deaths causally related to treatment / all	0 / 14	0 / 19	
Sudden cardiac death			
subjects affected / exposed	6 / 3001 (0.20%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 6	0 / 1	
Sudden death			
subjects affected / exposed	2 / 3001 (0.07%)	4 / 3050 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 2	0 / 4	
General physical health deterioration			
subjects affected / exposed	3 / 3001 (0.10%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Cardiac death			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Multi-organ failure			
subjects affected / exposed	1 / 3001 (0.03%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pyrexia			
subjects affected / exposed	5 / 3001 (0.17%)	5 / 3050 (0.16%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Social circumstances			

Elderly			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	37 / 3001 (1.23%)	33 / 3050 (1.08%)	
occurrences causally related to treatment / all	0 / 37	0 / 33	
deaths causally related to treatment / all	0 / 2	0 / 5	
Respiratory failure			
subjects affected / exposed	7 / 3001 (0.23%)	9 / 3050 (0.30%)	
occurrences causally related to treatment / all	0 / 7	0 / 9	
deaths causally related to treatment / all	0 / 5	0 / 3	
Pulmonary embolism			
subjects affected / exposed	25 / 3001 (0.83%)	31 / 3050 (1.02%)	
occurrences causally related to treatment / all	0 / 25	0 / 31	
deaths causally related to treatment / all	0 / 2	0 / 2	
Idiopathic pulmonary fibrosis			
subjects affected / exposed	2 / 3001 (0.07%)	4 / 3050 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 3	
Pneumonia aspiration			
subjects affected / exposed	2 / 3001 (0.07%)	4 / 3050 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pulmonary fibrosis			
subjects affected / exposed	2 / 3001 (0.07%)	5 / 3050 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 1	
Acute respiratory failure			
subjects affected / exposed	0 / 3001 (0.00%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	

Bronchial obstruction			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Chronic obstructive pulmonary disease			
subjects affected / exposed	27 / 3001 (0.90%)	29 / 3050 (0.95%)	
occurrences causally related to treatment / all	0 / 27	0 / 29	
deaths causally related to treatment / all	0 / 1	0 / 0	
Interstitial lung disease			
subjects affected / exposed	6 / 3001 (0.20%)	5 / 3050 (0.16%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Laryngeal oedema			
subjects affected / exposed	0 / 3001 (0.00%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumothorax			
subjects affected / exposed	2 / 3001 (0.07%)	0 / 3050 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	0 / 3001 (0.00%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory arrest			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Confusional state			
subjects affected / exposed	9 / 3001 (0.30%)	5 / 3050 (0.16%)	
occurrences causally related to treatment / all	0 / 9	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Delirium			
subjects affected / exposed	6 / 3001 (0.20%)	9 / 3050 (0.30%)	
occurrences causally related to treatment / all	0 / 6	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 1	
Korsakoff's psychosis alcoholic			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Investigations			
Heart rate irregular			
subjects affected / exposed	1 / 3001 (0.03%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	19 / 3001 (0.63%)	32 / 3050 (1.05%)	
occurrences causally related to treatment / all	0 / 19	0 / 32	
deaths causally related to treatment / all	0 / 0	0 / 1	
Femur fracture			
subjects affected / exposed	9 / 3001 (0.30%)	9 / 3050 (0.30%)	
occurrences causally related to treatment / all	0 / 9	0 / 9	
deaths causally related to treatment / all	0 / 1	0 / 1	
Alcohol poisoning			
subjects affected / exposed	2 / 3001 (0.07%)	4 / 3050 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cervical vertebral fracture			
subjects affected / exposed	1 / 3001 (0.03%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	

Head injury			
subjects affected / exposed	10 / 3001 (0.33%)	13 / 3050 (0.43%)	
occurrences causally related to treatment / all	0 / 10	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 1	
Multiple injuries			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Post procedural complication			
subjects affected / exposed	3 / 3001 (0.10%)	4 / 3050 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Road traffic accident			
subjects affected / exposed	2 / 3001 (0.07%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Spinal cord injury			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Subdural haematoma			
subjects affected / exposed	4 / 3001 (0.13%)	4 / 3050 (0.13%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	131 / 3001 (4.37%)	145 / 3050 (4.75%)	
occurrences causally related to treatment / all	3 / 131	0 / 145	
deaths causally related to treatment / all	0 / 0	0 / 2	
Cardiac failure			
subjects affected / exposed	41 / 3001 (1.37%)	52 / 3050 (1.70%)	
occurrences causally related to treatment / all	0 / 41	0 / 52	
deaths causally related to treatment / all	0 / 6	0 / 2	
Myocardial infarction			

subjects affected / exposed	40 / 3001 (1.33%)	45 / 3050 (1.48%)	
occurrences causally related to treatment / all	0 / 40	0 / 40	
deaths causally related to treatment / all	0 / 4	0 / 10	
Acute myocardial infarction			
subjects affected / exposed	22 / 3001 (0.73%)	50 / 3050 (1.64%)	
occurrences causally related to treatment / all	0 / 22	0 / 50	
deaths causally related to treatment / all	0 / 0	0 / 4	
Angina pectoris			
subjects affected / exposed	35 / 3001 (1.17%)	28 / 3050 (0.92%)	
occurrences causally related to treatment / all	0 / 35	2 / 28	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac arrest			
subjects affected / exposed	22 / 3001 (0.73%)	23 / 3050 (0.75%)	
occurrences causally related to treatment / all	0 / 22	0 / 23	
deaths causally related to treatment / all	0 / 16	0 / 16	
Cardiac disorder			
subjects affected / exposed	4 / 3001 (0.13%)	4 / 3050 (0.13%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 2	0 / 4	
Myocardial ischaemia			
subjects affected / exposed	6 / 3001 (0.20%)	14 / 3050 (0.46%)	
occurrences causally related to treatment / all	0 / 6	0 / 14	
deaths causally related to treatment / all	0 / 1	0 / 5	
Cardiac failure congestive			
subjects affected / exposed	17 / 3001 (0.57%)	17 / 3050 (0.56%)	
occurrences causally related to treatment / all	0 / 17	0 / 17	
deaths causally related to treatment / all	0 / 1	0 / 2	
Left ventricular dysfunction			
subjects affected / exposed	8 / 3001 (0.27%)	12 / 3050 (0.39%)	
occurrences causally related to treatment / all	0 / 8	0 / 12	
deaths causally related to treatment / all	0 / 1	0 / 1	
Acute coronary syndrome			

subjects affected / exposed	3 / 3001 (0.10%)	3 / 3050 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Atrioventricular block			
subjects affected / exposed	3 / 3001 (0.10%)	5 / 3050 (0.16%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure chronic			
subjects affected / exposed	2 / 3001 (0.07%)	0 / 3050 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coronary artery disease			
subjects affected / exposed	10 / 3001 (0.33%)	12 / 3050 (0.39%)	
occurrences causally related to treatment / all	0 / 10	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 1	
Heart valve incompetence			
subjects affected / exposed	3 / 3001 (0.10%)	0 / 3050 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 3001 (0.00%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Left ventricular hypertrophy			
subjects affected / exposed	1 / 3001 (0.03%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pericardial haemorrhage			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Right ventricular failure			

subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ventricular fibrillation			
subjects affected / exposed	2 / 3001 (0.07%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	7 / 3001 (0.23%)	5 / 3050 (0.16%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	38 / 3001 (1.27%)	44 / 3050 (1.44%)	
occurrences causally related to treatment / all	0 / 38	0 / 44	
deaths causally related to treatment / all	0 / 7	0 / 4	
Transient ischaemic attack			
subjects affected / exposed	33 / 3001 (1.10%)	47 / 3050 (1.54%)	
occurrences causally related to treatment / all	0 / 33	0 / 47	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	8 / 3001 (0.27%)	16 / 3050 (0.52%)	
occurrences causally related to treatment / all	0 / 8	0 / 16	
deaths causally related to treatment / all	0 / 2	0 / 1	
Cerebral haemorrhage			
subjects affected / exposed	1 / 3001 (0.03%)	3 / 3050 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Cerebral haematoma			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Coma hepatic			

subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Convulsion			
subjects affected / exposed	2 / 3001 (0.07%)	4 / 3050 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dementia with Lewy bodies			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Encephalopathy			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemorrhage intracranial			
subjects affected / exposed	2 / 3001 (0.07%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Motor neurone disease			
subjects affected / exposed	2 / 3001 (0.07%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Spinal cord depression			
subjects affected / exposed	3 / 3001 (0.10%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	3 / 3001 (0.10%)	3 / 3050 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Blood and lymphatic system disorders			
Anaemia haemolytic autoimmune			

subjects affected / exposed	2 / 3001 (0.07%)	0 / 3050 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	121 / 3001 (4.03%)	140 / 3050 (4.59%)	
occurrences causally related to treatment / all	0 / 121	0 / 140	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	7 / 3001 (0.23%)	14 / 3050 (0.46%)	
occurrences causally related to treatment / all	0 / 7	0 / 14	
deaths causally related to treatment / all	0 / 2	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	1 / 3001 (0.03%)	3 / 3050 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pancreatitis			
subjects affected / exposed	12 / 3001 (0.40%)	9 / 3050 (0.30%)	
occurrences causally related to treatment / all	2 / 12	0 / 9	
deaths causally related to treatment / all	1 / 1	0 / 1	
Abdominal pain			
subjects affected / exposed	11 / 3001 (0.37%)	30 / 3050 (0.98%)	
occurrences causally related to treatment / all	0 / 11	0 / 30	
deaths causally related to treatment / all	0 / 0	0 / 1	
Colitis ischaemic			
subjects affected / exposed	3 / 3001 (0.10%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Diarrhoea			
subjects affected / exposed	14 / 3001 (0.47%)	8 / 3050 (0.26%)	
occurrences causally related to treatment / all	3 / 14	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gallstone ileus			

subjects affected / exposed	0 / 3001 (0.00%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastritis erosive			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal perforation			
subjects affected / exposed	1 / 3001 (0.03%)	0 / 3050 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pancreatitis acute			
subjects affected / exposed	3 / 3001 (0.10%)	6 / 3050 (0.20%)	
occurrences causally related to treatment / all	1 / 3	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	8 / 3001 (0.27%)	11 / 3050 (0.36%)	
occurrences causally related to treatment / all	0 / 8	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 1	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	3 / 3001 (0.10%)	4 / 3050 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	6 / 3001 (0.20%)	7 / 3050 (0.23%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 2	
Hepatic cirrhosis			
subjects affected / exposed	7 / 3001 (0.23%)	8 / 3050 (0.26%)	
occurrences causally related to treatment / all	0 / 7	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 1	
Alcoholic liver disease			

subjects affected / exposed	1 / 3001 (0.03%)	4 / 3050 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cholecystitis			
subjects affected / exposed	10 / 3001 (0.33%)	18 / 3050 (0.59%)	
occurrences causally related to treatment / all	2 / 10	0 / 18	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cirrhosis alcoholic			
subjects affected / exposed	4 / 3001 (0.13%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatic failure			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	43 / 3001 (1.43%)	22 / 3050 (0.72%)	
occurrences causally related to treatment / all	1 / 43	0 / 22	
deaths causally related to treatment / all	0 / 4	0 / 2	
Renal failure			
subjects affected / exposed	6 / 3001 (0.20%)	13 / 3050 (0.43%)	
occurrences causally related to treatment / all	1 / 6	0 / 13	
deaths causally related to treatment / all	0 / 2	0 / 2	
Renal failure chronic			
subjects affected / exposed	8 / 3001 (0.27%)	7 / 3050 (0.23%)	
occurrences causally related to treatment / all	0 / 8	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 2	
Renal impairment			
subjects affected / exposed	5 / 3001 (0.17%)	10 / 3050 (0.33%)	
occurrences causally related to treatment / all	0 / 5	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 2	
Cystitis haemorrhagic			

subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Proteinuria			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal disorder			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	101 / 3001 (3.37%)	109 / 3050 (3.57%)	
occurrences causally related to treatment / all	0 / 101	0 / 109	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	0 / 3001 (0.00%)	3 / 3050 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Rheumatoid arthritis			
subjects affected / exposed	4 / 3001 (0.13%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Infections and infestations			
Pneumonia			
subjects affected / exposed	92 / 3001 (3.07%)	127 / 3050 (4.16%)	
occurrences causally related to treatment / all	0 / 92	0 / 127	
deaths causally related to treatment / all	0 / 9	0 / 14	
Lower respiratory tract infection			
subjects affected / exposed	29 / 3001 (0.97%)	43 / 3050 (1.41%)	
occurrences causally related to treatment / all	0 / 29	0 / 43	
deaths causally related to treatment / all	0 / 1	0 / 2	

Urinary tract infection			
subjects affected / exposed	29 / 3001 (0.97%)	38 / 3050 (1.25%)	
occurrences causally related to treatment / all	0 / 29	0 / 38	
deaths causally related to treatment / all	0 / 0	0 / 3	
Sepsis			
subjects affected / exposed	19 / 3001 (0.63%)	38 / 3050 (1.25%)	
occurrences causally related to treatment / all	0 / 19	0 / 38	
deaths causally related to treatment / all	0 / 4	0 / 11	
Urosepsis			
subjects affected / exposed	16 / 3001 (0.53%)	14 / 3050 (0.46%)	
occurrences causally related to treatment / all	0 / 16	0 / 14	
deaths causally related to treatment / all	0 / 2	0 / 1	
Bronchopneumonia			
subjects affected / exposed	2 / 3001 (0.07%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Neutropenic sepsis			
subjects affected / exposed	1 / 3001 (0.03%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pneumonia bacterial			
subjects affected / exposed	0 / 3001 (0.00%)	2 / 3050 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Bacterial infection			
subjects affected / exposed	2 / 3001 (0.07%)	3 / 3050 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cellulitis			
subjects affected / exposed	21 / 3001 (0.70%)	22 / 3050 (0.72%)	
occurrences causally related to treatment / all	0 / 21	0 / 22	
deaths causally related to treatment / all	0 / 0	0 / 1	
Creutzfeldt-Jakob disease			

subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Endocarditis			
subjects affected / exposed	3 / 3001 (0.10%)	3 / 3050 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Erysipelas			
subjects affected / exposed	15 / 3001 (0.50%)	14 / 3050 (0.46%)	
occurrences causally related to treatment / all	0 / 15	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 1	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	8 / 3001 (0.27%)	9 / 3050 (0.30%)	
occurrences causally related to treatment / all	0 / 8	0 / 9	
deaths causally related to treatment / all	0 / 1	0 / 0	
Liver abscess			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Peritonitis bacterial			
subjects affected / exposed	1 / 3001 (0.03%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia viral			
subjects affected / exposed	1 / 3001 (0.03%)	0 / 3050 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Post procedural infection			
subjects affected / exposed	8 / 3001 (0.27%)	8 / 3050 (0.26%)	
occurrences causally related to treatment / all	0 / 8	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	
Post procedural sepsis			

subjects affected / exposed	3 / 3001 (0.10%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyelonephritis			
subjects affected / exposed	5 / 3001 (0.17%)	6 / 3050 (0.20%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Septic shock			
subjects affected / exposed	0 / 3001 (0.00%)	3 / 3050 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	45 / 3001 (1.50%)	64 / 3050 (2.10%)	
occurrences causally related to treatment / all	0 / 45	0 / 64	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hyperkalaemia			
subjects affected / exposed	9 / 3001 (0.30%)	9 / 3050 (0.30%)	
occurrences causally related to treatment / all	0 / 9	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 2	
Calcium metabolism disorder			
subjects affected / exposed	0 / 3001 (0.00%)	1 / 3050 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Diabetes mellitus			
subjects affected / exposed	9 / 3001 (0.30%)	13 / 3050 (0.43%)	
occurrences causally related to treatment / all	0 / 9	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 1	
Diabetic ketoacidosis			

subjects affected / exposed	1 / 3001 (0.03%)	0 / 3050 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Febuxostat (safety population) - during the treatment period	Allopurinol (safety population) - during the treatment period	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	686 / 3001 (22.86%)	132 / 3050 (4.33%)	
Investigations			
Liver function test abnormal			
subjects affected / exposed	48 / 3001 (1.60%)	5 / 3050 (0.16%)	
occurrences (all)	48	5	
Nervous system disorders			
Headache			
subjects affected / exposed	62 / 3001 (2.07%)	9 / 3050 (0.30%)	
occurrences (all)	62	9	
Dizziness			
subjects affected / exposed	41 / 3001 (1.37%)	14 / 3050 (0.46%)	
occurrences (all)	41	14	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	48 / 3001 (1.60%)	3 / 3050 (0.10%)	
occurrences (all)	48	3	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	154 / 3001 (5.13%)	18 / 3050 (0.59%)	
occurrences (all)	154	18	
Nausea			
subjects affected / exposed	55 / 3001 (1.83%)	5 / 3050 (0.16%)	
occurrences (all)	55	5	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	31 / 3001 (1.03%)	4 / 3050 (0.13%)	
occurrences (all)	31	4	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	60 / 3001 (2.00%)	20 / 3050 (0.66%)	
occurrences (all)	60	20	
Pruritus			
subjects affected / exposed	32 / 3001 (1.07%)	12 / 3050 (0.39%)	
occurrences (all)	32	12	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	46 / 3001 (1.53%)	9 / 3050 (0.30%)	
occurrences (all)	46	9	
Pain in extremity			
subjects affected / exposed	39 / 3001 (1.30%)	9 / 3050 (0.30%)	
occurrences (all)	39	9	
Myalgia			
subjects affected / exposed	32 / 3001 (1.07%)	4 / 3050 (0.13%)	
occurrences (all)	32	4	
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	38 / 3001 (1.27%)	20 / 3050 (0.66%)	
occurrences (all)	38	20	

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

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

The study was slightly underpowered at approximately 77% power to exclude a non-inferiority limit of 1.3 or alternatively alternatively, 80% power to exclude a non-inferiority limit of 1.315. The impact is considered modest.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33181081