



Clinical trial results:

(OSKIRA-X): A Long-term Extension Study to Assess the Safety and Efficacy of Fostamatinib Disodium in the Treatment of Rheumatoid Arthritis

These results have been removed from public view whilst they are reviewed and may need to be corrected before being returned to public view

Summary

EudraCT number	2010-020892-22
Trial protocol	BE GB DE SK HU LV EE LT CZ PT ES BG IT NL
Global end of trial date	18 September 2013

Results information

Result version number	v1 (current)
This version publication date	23 December 2016
First version publication date	23 December 2016

Trial information

Trial identification

Sponsor protocol code	D4300C00005
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01242514
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca Pharmaceuticals
Sponsor organisation address	Alderley Park, Macclesfield, United Kingdom, SK10 4TG
Public contact	Neil Mackillop, AstraZeneca, information.center@astrazeneca.com
Scientific contact	Neil Mackillop, AstraZeneca, neil.mackillop@astrazeneca.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 October 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 September 2013
Global end of trial reached?	Yes
Global end of trial date	18 September 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the long-term safety and tolerability of fostamatinib in patients with active RA by assessment of adverse event (AE) reports, laboratory safety data, vital signs, electrocardiograms (ECGs) and physical examination.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Conference on Harmonisation/Good Clinical Practice (GCP) and applicable regulatory requirements and the AstraZeneca policy on Bioethics and Human Biological Samples.

Before enrolment of any patient into the study, the final clinical study protocol, including the final version of the informed consent form, was approved by the national regulatory authority or a notification to the national regulatory authority was done, according to local regulations. The study was approved or given a favourable opinion in writing by an Independent Ethics Committee (IEC) for each study centre.

The investigator(s) at each centre ensured that the patient was given full and adequate oral and written information about the nature, purpose, possible risk and benefit of the study. Patients were also notified that they were free to discontinue investigational product (IP) and/or withdraw from the study at any time. The patient was given the opportunity to ask questions and allowed time to consider the information provided. The patient's signed and dated informed consent was obtained before conducting any procedure specifically for the study.

Background therapy:

Patients entering from qualifying studies D4300C00001, D4300C00002, D4300C00003 and D4300C00033 were to continue taking their study treatment in combination with their regular DMARD therapy, at the discretion of the investigator. Depending on the qualifying study, this could be methotrexate, sulfasalazine, hydroxychloroquine or chloroquine. Patients entering from qualifying study D4300C00004 were to continue taking IP as monotherapy, though it was acceptable to initiate an allowed DMARD, at the discretion of the investigator.

Evidence for comparator: -

Actual start date of recruitment	10 January 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 453
Country: Number of subjects enrolled	Ukraine: 201

Country: Number of subjects enrolled	Czech Republic: 165
Country: Number of subjects enrolled	Argentina: 133
Country: Number of subjects enrolled	Poland: 120
Country: Number of subjects enrolled	South Africa: 103
Country: Number of subjects enrolled	India: 124
Country: Number of subjects enrolled	Peru: 116
Country: Number of subjects enrolled	Serbia: 81
Country: Number of subjects enrolled	Mexico: 76
Country: Number of subjects enrolled	Bulgaria: 50
Country: Number of subjects enrolled	Hungary: 38
Country: Number of subjects enrolled	Russian Federation: 30
Country: Number of subjects enrolled	Canada: 24
Country: Number of subjects enrolled	United Kingdom: 30
Country: Number of subjects enrolled	Brazil: 20
Country: Number of subjects enrolled	Estonia: 21
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	Israel: 19
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	Latvia: 13
Country: Number of subjects enrolled	Lithuania: 16
Country: Number of subjects enrolled	Slovakia: 11
Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Chile: 4
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Portugal: 6
Country: Number of subjects enrolled	Romania: 3
Worldwide total number of subjects	1912
EEA total number of subjects	519

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)	1617
From 65 to 84 years	294
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Total of 1917 enrolled patients: 1346, 357 & 214 were allocated to the 100 mg twice daily (bid), 150 mg once daily (qd) and 100 mg qd groups, respectively (1343, 357 & 212 received at least 1 dose of investigational product). As this was a long-term extension study no specific end date was given. As such no patients were recorded as completers.

Pre-assignment

Screening details:

A total of 5 patients did not receive treatment.

Period 1

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

Blinding implementation details:

Blinding of the treatment regimens was necessary initially, since the randomised, double-blind, placebo-controlled qualifying studies were ongoing when this extension study commenced. Once the qualifying studies were completed and database was locked, the treatment allocation could be considered open-label.

Arms

Are arms mutually exclusive?	Yes
Arm title	Fostamatinib 100 mg bid

Arm description:

Oral treatment

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

Dosage and administration details:

100mg twice daily

Arm title	Fostamatinib 150 mg qd
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Arm description:

Oral treatment

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

Dosage and administration details:

150mg once daily

Arm title	Fostamatinib 100 mg qd
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Arm description:

Oral treatment

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

Dosage and administration details:

100mg once daily

Number of subjects in period 1	Fostamatinib 100 mg bid	Fostamatinib 150 mg qd	Fostamatinib 100 mg qd
Started	1343	357	212
Completed	985	303	162
Not completed	358	54	50
Other eg Subject decision	90	10	11
Severe non-compliance to protocol	5	2	1
Lack of therapeutic response	99	16	10
Adverse event, non-fatal	129	18	19
Dev. of study specific discontin. criteria	21	3	5
Lost to follow-up	14	5	4

Baseline characteristics

Reporting groups

Reporting group title	Fostamatinib 100 mg bid
Reporting group description:	
Oral treatment	
Reporting group title	Fostamatinib 150 mg qd
Reporting group description:	
Oral treatment	
Reporting group title	Fostamatinib 100 mg qd
Reporting group description:	
Oral treatment	

Reporting group values	Fostamatinib 100 mg bid	Fostamatinib 150 mg qd	Fostamatinib 100 mg qd
Number of subjects	1343	357	212
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)	1138	295	184
From 65-84 years	204	62	28
85 years and over	1	0	0
Age Continuous			
Units: years			
arithmetic mean	53	53	53
standard deviation	± 12	± 11.6	± 11.3
Gender, Male/Female			
Units: Participants			
Female	1086	297	193
Male	257	60	19
Race/Ethnicity, Customized			
Units: Subjects			
White	1092	278	141
Black or African American	63	11	6
Asian	40	12	7
American Indian or Alaska Native	20	11	6
Indian or Pakistani	54	15	22
Other	74	30	30

Reporting group values	Total		
Number of subjects	1912		

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)	1617		
From 65-84 years	294		
85 years and over	1		
Age Continuous Units: years arithmetic mean standard deviation	-		
Gender, Male/Female Units: Participants			
Female	1576		
Male	336		
Race/Ethnicity, Customized Units: Subjects			
White	1511		
Black or African American	80		
Asian	59		
American Indian or Alaska Native	37		
Indian or Pakistani	91		
Other	134		

Subject analysis sets

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

All patients who receive at least 1 dose of study drug and summarised according to treatment first received in this study.

Reporting group values	Full Analysis Set		
Number of subjects	1912		
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)	1617		
From 65-84 years	294		
85 years and over	1		

Age Continuous Units: years arithmetic mean standard deviation	53 ± 11.8		
Gender, Male/Female Units: Participants			
Female	1576		
Male	336		
Race/Ethnicity, Customized Units: Subjects			
White	1511		
Black or African American	80		
Asian	59		
American Indian or Alaska Native	37		
Indian or Pakistani	91		
Other	134		

End points

End points reporting groups

Reporting group title	Fostamatinib 100 mg bid
Reporting group description:	
Oral treatment	
Reporting group title	Fostamatinib 150 mg qd
Reporting group description:	
Oral treatment	
Reporting group title	Fostamatinib 100 mg qd
Reporting group description:	
Oral treatment	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients who receive at least 1 dose of study drug and summarised according to treatment first received in this study.	

Primary: Percentage of patients who had at least 1 adverse event in any category

End point title	Percentage of patients who had at least 1 adverse event in any category ^[1]
End point description:	
AE = adverse event, bid = twice daily, IP = investigational product, qd = once daily, SAE = serious adverse event	
End point type	Primary
End point timeframe:	
Entry in extension to end of study (variable duration; maximum 109 weeks)	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.	
Justification: No statistical analyses - observational study.	

End point values	Fostamatinib 100 mg bid	Fostamatinib 150 mg qd	Fostamatinib 100 mg qd	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1343	357	212	
Units: Percentage of patients				
number (not applicable)				
Any AE	74.4	70.3	69.8	
Any AE with outcome of death	0.7	0.3	0.5	
Any SAE (including events with outcome of death)	11.4	8.7	5.7	
Any AE leading to discontinuation of IP	10.5	5.9	9.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean DAS28-CRP score

End point title	Mean DAS28-CRP score
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End point description:

DAS28-CRP: Disease Activity Score based on a count of swollen and tender joints (out of 28 joints), blood test measures of inflammation (CRP) and the patient's own assessment. Scores can take any positive value with a lower value indicating a better clinical condition. Number of participants are those with data at entry to this study (Week 0). As no imputation was applied, the numbers at subsequent visits are lower. bid = twice daily, CRP = C-reactive protein, qd = once daily

End point type	Secondary
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End point timeframe:

Weeks 0, 12, 24, 36 and 52

End point values	Fostamatinib 100 mg bid	Fostamatinib 150 mg qd	Fostamatinib 100 mg qd	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1247	336	198	
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=1247, 336, 198)	4.5 (± 1.58)	3.8 (± 1.24)	3.9 (± 1.27)	
Week 12 (n=1018, 288, 160)	3.8 (± 1.34)	3.6 (± 1.19)	3.7 (± 1.21)	
Week 24 (n=800, 230 126)	3.8 (± 1.3)	3.7 (± 1.24)	3.6 (± 1.19)	
Week 36 (n=581, 148, 68)	3.9 (± 1.32)	3.7 (± 1.24)	3.9 (± 1.07)	
Week 52 (n=290, 28, 14)	4 (± 1.25)	3.8 (± 1.37)	3.6 (± 1.22)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean mTSS score

End point title	Mean mTSS score
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End point description:

mTSS: modified total sharp score, a measure of structural progression based upon X-rays. Hand and foot joints are scored for erosions and joint space narrowing and the results summed to give a value between 0 and 488. A higher value represents more serious progression of the disease. Number of participants are those with data at entry to this study (Week 0). As no imputation was applied, the numbers at subsequent visits are lower. bid = twice daily, N/A = not applicable, qd = once daily

End point type	Secondary
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End point timeframe:

Weeks 0 and 52

End point values	Fostamatinib 100 mg bid	Fostamatinib 150 mg qd	Fostamatinib 100 mg qd	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	480	73 ^[2]	37	
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=480, 73, 37)	30.5 (± 47.73)	22.2 (± 32.89)	20.8 (± 46.6)	
Week 52 (n=223, 1, 6)	30.1 (± 46.83)	0.5 (± 0)	37.3 (± 67.7)	

Notes:

[2] - 0 entered for standard deviation, although not defined for a single patient

Statistical analyses

No statistical analyses for this end point

Secondary: Mean HAQ-DI score

End point title	Mean HAQ-DI score
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End point description:

HAQ-DI: Health Assessment Questionnaire - Disability Index, a measure of physical function. The HAQ-DI score is then calculated by summing the category scores from 8 sub-categories (ie, scores for patient ability in dressing and grooming, rising, eating, walking, hygiene, reach, grip and common daily activities) and dividing by the number of categories completed. The HAQ-DI score takes values between 0 and 3, with a higher score indicating greater disability. Number of participants are those with data at entry to this study (Week 0). As no imputation was applied, the numbers at subsequent visits are lower. bid = twice daily, qd = once daily

End point type	Secondary
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End point timeframe:

Weeks 0, 12, 24, 36 and 52

End point values	Fostamatinib 100 mg bid	Fostamatinib 150 mg qd	Fostamatinib 100 mg qd	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1271	342	201	
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=1271, 342, 201)	1.2 (± 0.69)	1 (± 0.64)	1 (± 0.62)	
Week 12 (n=1061, 298, 166)	1.1 (± 0.68)	1 (± 0.63)	1 (± 0.63)	
Week 24 (n=817, 238, 132)	1.1 (± 0.68)	1 (± 0.67)	0.9 (± 0.55)	
Week 36 (n=587, 149, 71)	1.1 (± 0.67)	1 (± 0.65)	1.1 (± 0.62)	
Week 52 (n=296, 28, 14)	1.2 (± 0.68)	1.1 (± 0.64)	1 (± 0.73)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

As this was an ongoing long term extension study the timeframe for adverse event reporting was from the start of the study (January 2011) to study termination (September 2013).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	15.1
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Reporting groups

Reporting group title	FOSTA 100 MG BID
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Reporting group description:

Fostamatinib 100mg twice daily

Reporting group title	FOSTA 150 MG QD
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Reporting group description:

Fostamatinib 150mg once daily

Reporting group title	FOSTA 100 MG QD
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Reporting group description:

Fostamatinib 100mg once daily

Serious adverse events	FOSTA 100 MG BID	FOSTA 150 MG QD	FOSTA 100 MG QD
Total subjects affected by serious adverse events			
subjects affected / exposed	153 / 1343 (11.39%)	31 / 357 (8.68%)	12 / 212 (5.66%)
number of deaths (all causes)	9	1	1
number of deaths resulting from adverse events	2	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA			
subjects affected / exposed	2 / 1343 (0.15%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BENIGN NEOPLASM OF PROSTATE			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BENIGN SOFT TISSUE NEOPLASM			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

BREAST CANCER			
subjects affected / exposed	2 / 1343 (0.15%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CERVIX CARCINOMA			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLORECTAL CANCER			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC CANCER			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIPOMA			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG SQUAMOUS CELL CARCINOMA STAGE UNSPECIFIED			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MALIGNANT MELANOMA			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATIC NEUROENDOCRINE TUMOUR			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROSTATE CANCER			

subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL CANCER			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL CANCER METASTATIC			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL CELL CARCINOMA			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UTERINE LEIOMYOMA			
subjects affected / exposed	2 / 1343 (0.15%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VAGINAL CANCER			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
AORTIC ANEURYSM RUPTURE			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
AORTIC STENOSIS			
subjects affected / exposed	0 / 1343 (0.00%)	0 / 357 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AORTIC THROMBOSIS			

subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTERIAL THROMBOSIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMORAL ARTERY OCCLUSION			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ISCHAEMIA			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THROMBOPHLEBITIS SUPERFICIAL			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
DEVICE DISLOCATION			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	3 / 1343 (0.22%)	0 / 357 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			

ANAPHYLACTIC SHOCK			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOOD ALLERGY			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERSENSITIVITY			
subjects affected / exposed	2 / 1343 (0.15%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
ADENOMYOSIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OVARIAN CYST			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UTERINE POLYP			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			

subjects affected / exposed	2 / 1343 (0.15%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	1 / 1343 (0.07%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERVENTILATION			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA ASPIRATION			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
PULMONARY EMBOLISM			
subjects affected / exposed	4 / 1343 (0.30%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
RESPIRATORY FAILURE			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
ADJUSTMENT DISORDER			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ALCOHOL ABUSE			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEPRESSION			

subjects affected / exposed	2 / 1343 (0.15%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
LIVER FUNCTION TEST ABNORMAL			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ACCIDENTAL OVERDOSE			
subjects affected / exposed	0 / 1343 (0.00%)	2 / 357 (0.56%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FACIAL BONES FRACTURE			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMORAL NECK FRACTURE			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMUR FRACTURE			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FIBULA FRACTURE			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HUMERUS FRACTURE			
subjects affected / exposed	2 / 1343 (0.15%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

JOINT DISLOCATION			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
JOINT INJURY			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PATELLA FRACTURE			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TENDON RUPTURE			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TIBIA FRACTURE			
subjects affected / exposed	0 / 1343 (0.00%)	0 / 357 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ULNA FRACTURE			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER LIMB FRACTURE			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND DEHISCENCE			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WRIST FRACTURE			

subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA UNSTABLE			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL FIBRILLATION			
subjects affected / exposed	2 / 1343 (0.15%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRADYCARDIA			
subjects affected / exposed	0 / 1343 (0.00%)	0 / 357 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE CHRONIC			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	2 / 1343 (0.15%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIOMYOPATHY			

subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL INFARCTION			
subjects affected / exposed	2 / 1343 (0.15%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
APHASIA			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CAROTID ARTERY STENOSIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONVULSION			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSARTHRIA			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHAGIC STROKE			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
HYPERTENSIVE ENCEPHALOPATHY			

subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOGLYCAEMIC COMA			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ISCHAEMIC STROKE			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUMBAR RADICULOPATHY			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RADICULITIS LUMBOSACRAL			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SCIATICA			
subjects affected / exposed	0 / 1343 (0.00%)	0 / 357 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNCOPE			
subjects affected / exposed	3 / 1343 (0.22%)	2 / 357 (0.56%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TENSION HEADACHE			

subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VITH NERVE PARALYSIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
SPLENIC INFARCTION			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
RETINAL DETACHMENT			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 1343 (0.00%)	0 / 357 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE ABDOMEN			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

BARRETT'S OESOPHAGUS			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLITIS			
subjects affected / exposed	2 / 1343 (0.15%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLITIS MICROSCOPIC			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLONIC STENOSIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	4 / 1343 (0.30%)	0 / 357 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	2 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPEPSIA			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC ULCER			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRITIS			
subjects affected / exposed	2 / 1343 (0.15%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRITIS EROSIIVE			

subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATEMESIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEITIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEUS			
subjects affected / exposed	2 / 1343 (0.15%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INGUINAL HERNIA			
subjects affected / exposed	2 / 1343 (0.15%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL ISCHAEMIA			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL OBSTRUCTION			

subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
OESOPHAGEAL ACHALASIA			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATIC PSEUDOCYST			
subjects affected / exposed	0 / 1343 (0.00%)	0 / 357 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS			
subjects affected / exposed	3 / 1343 (0.22%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS ACUTE			
subjects affected / exposed	3 / 1343 (0.22%)	0 / 357 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hepatobiliary disorders			
BILE DUCT OBSTRUCTION			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BILIARY COLIC			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLECYSTITIS			
subjects affected / exposed	2 / 1343 (0.15%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLECYSTITIS ACUTE			

subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLECYSTITIS CHRONIC			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLELITHIASIS			
subjects affected / exposed	4 / 1343 (0.30%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GALLBLADDER POLYP			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POST CHOLECYSTECTOMY SYNDROME			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
DIGITAL ULCER			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ERYTHEMA MULTIFORME			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOXIC EPIDERMAL NECROLYSIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Renal and urinary disorders			

CALCULUS URETERIC			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CALCULUS URINARY			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEPHROLITHIASIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL FAILURE ACUTE			
subjects affected / exposed	3 / 1343 (0.22%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL IMPAIRMENT			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY BLADDER POLYP			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
GOITRE			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
ARTHRITIS			
subjects affected / exposed	2 / 1343 (0.15%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

BACK PAIN			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIP DEFORMITY			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERVERTEBRAL DISC DISORDER			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERVERTEBRAL DISC DISPLACEMENT			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	4 / 1343 (0.30%)	0 / 357 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUMBAR SPINAL STENOSIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEITIS			
subjects affected / exposed	0 / 1343 (0.00%)	0 / 357 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOARTHRITIS			

subjects affected / exposed	6 / 1343 (0.45%)	2 / 357 (0.56%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEONECROSIS			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PATHOLOGICAL FRACTURE			
subjects affected / exposed	2 / 1343 (0.15%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RHEUMATOID ARTHRITIS			
subjects affected / exposed	9 / 1343 (0.67%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 11	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SJOGREN'S SYNDROME			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPONDYLOLISTHESIS			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNOVITIS			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABSCCESS LIMB			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
APPENDICITIS			

subjects affected / exposed	4 / 1343 (0.30%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTHRITIS BACTERIAL			
subjects affected / exposed	0 / 1343 (0.00%)	0 / 357 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERAEMIA			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERIAL PYELONEPHRITIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERIAL SEPSIS			
subjects affected / exposed	2 / 1343 (0.15%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHOPNEUMONIA			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	6 / 1343 (0.45%)	0 / 357 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	2 / 7	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CYTOMEGALOVIRUS INFECTION			

subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTEROCOLITIS BACTERIAL			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTEROCOLITIS VIRAL			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ERYSIPELAS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA URINARY TRACT INFECTION			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GANGRENE			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS BACTERIAL			

subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS VIRAL			
subjects affected / exposed	1 / 1343 (0.07%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES ZOSTER			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERVERTEBRAL DISCITIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIVER ABSCESS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
LUNG ABSCESS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOMYELITIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OTITIS EXTERNA			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS VIRAL			

subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERITONITIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	5 / 1343 (0.37%)	1 / 357 (0.28%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	1 / 5	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA BACTERIAL			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA VIRAL			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
PULMONARY TUBERCULOSIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			

subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION BACTERIAL			
subjects affected / exposed	2 / 1343 (0.15%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UROSEPSIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND INFECTION BACTERIAL			
subjects affected / exposed	0 / 1343 (0.00%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND SEPSIS			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	1 / 1343 (0.07%)	0 / 357 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOKALAEMIA			
subjects affected / exposed	1 / 1343 (0.07%)	1 / 357 (0.28%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPONATRAEMIA			

subjects affected / exposed	1 / 1343 (0.07%)	1 / 357 (0.28%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TYPE 2 DIABETES MELLITUS			
subjects affected / exposed	0 / 1343 (0.00%)	0 / 357 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	FOSTA 100 MG BID	FOSTA 150 MG QD	FOSTA 100 MG QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	466 / 1343 (34.70%)	98 / 357 (27.45%)	68 / 212 (32.08%)
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	166 / 1343 (12.36%)	20 / 357 (5.60%)	14 / 212 (6.60%)
occurrences (all)	197	23	15
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	202 / 1343 (15.04%)	43 / 357 (12.04%)	28 / 212 (13.21%)
occurrences (all)	268	61	40
Musculoskeletal and connective tissue disorders			
RHEUMATOID ARTHRITIS			
subjects affected / exposed	116 / 1343 (8.64%)	30 / 357 (8.40%)	19 / 212 (8.96%)
occurrences (all)	155	35	22
Infections and infestations			
NASOPHARYNGITIS			
subjects affected / exposed	86 / 1343 (6.40%)	28 / 357 (7.84%)	15 / 212 (7.08%)
occurrences (all)	102	31	16

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 March 2011	Restrictions for male patients entering the study who wished to father a child or donate sperm were removed.
04 October 2011	If in the investigator's opinion the patient had achieved sustained stable RA disease activity then reduction of NSAIDs / steroids was permitted.
17 January 2012	The addition of patients who could enter from qualifying study D4300C00033 with an exploratory objective to describe the effects on blood pressure in these patients.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported