Clinical trial results:
Phase 3b/4 Randomized Safety Endpoint Study of 2 Doses of Tofacitinib in Comparison to a Tumor Necrosis Factor (TNF) Inhibitor in Subjects with Rheumatoid Arthritis

Summary

EudraCT number	2013-003177-99
Trial protocol	CZ SE FI NL SK GB ES AT
Global end of trial date	22 July 2020

Results information

Result version number	v1 (current)
This version publication date	06 August 2021
First version publication date	06 August 2021

Trial information

Trial identification

Sponsor protocol code	A3921133

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02092467
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 May 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety of tofacitinib at two doses versus tumor necrosis factor inhibitor (TNFi).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy:

All subjects were enrolled taking background methotrexate.

Evidence for comparator: -

Actual start date of recruitment	14 March 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 253
Country: Number of subjects enrolled	Australia: 53
Country: Number of subjects enrolled	Brazil: 251
Country: Number of subjects enrolled	Bulgaria: 81
Country: Number of subjects enrolled	Canada: 67
Country: Number of subjects enrolled	Chile: 96
Country: Number of subjects enrolled	China: 2
Country: Number of subjects enrolled	Colombia: 107
Country: Number of subjects enrolled	Czechia: 262
Country: Number of subjects enrolled	Finland: 9
Country: Number of subjects enrolled	Hong Kong: 25
Country: Number of subjects enrolled	Israel: 157
Country: Number of subjects enrolled	Jordan: 13
Country: Number of subjects enrolled	Lebanon: 4
Country: Number of subjects enrolled	Malaysia: 18
Country: Number of subjects enrolled	Mexico: 580
Country: Number of subjects enrolled	Netherlands: 13
Country: Number of subjects enrolled	New Zealand: 23
Country: Number of subjects enrolled	Peru: 308
Country: Number of subjects enrolled	Poland: 1124

Country: Number of subjects enrolled	Puerto Rico: 8
Country: Number of subjects enrolled	Russian Federation: 229
Country: Number of subjects enrolled	Slovakia: 64
Country: Number of subjects enrolled	South Africa: 412
Country: Number of subjects enrolled	Spain: 87
Country: Number of subjects enrolled	Taiwan: 69
Country: Number of subjects enrolled	Thailand: 82
Country: Number of subjects enrolled	Turkey: 44
Country: Number of subjects enrolled	United Kingdom: 83
Country: Number of subjects enrolled	United States: 2035
Worldwide total number of subjects	6559
EEA total number of subjects	1640

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)	4204
From 65 to 84 years	2321
85 years and over	34

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Study started from 14 March 2014 and completed on 22 July 2020.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Tofacitinib 5 mg BID

Arm description:

Subjects received tofacitinib 5 milligram (mg) oral tablet twice daily (BID) up to 72 months. Subjects were followed up for at least 28 days after last dose of study drug.

Arm type	Experimental
Investigational medicinal product name	Tofacitinib
Investigational medicinal product code	
Other name	CP-690,550
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received tofacitinib 5 mg tablet orally BID.

Arm title	Tofacitinib 10 mg BID

Arm description:

Subjects received tofacitinib 10 mg oral tablets (two tablets of 5 mg each) BID up to 72 months. Dose was reduced to tofacitinib 5 mg BID on or after 19 February 2019 as per Study Protocol Amendment 8. Subjects were followed up for at least 28 days after last dose of study drug.

Arm type	Experimental
Investigational medicinal product name	Tofacitinib
Investigational medicinal product code	
Other name	CP-690,550
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received tofacitinib 10 mg tablet orally BID.

Arm title	TNFi

Arm description:

In the United States (US), Puerto Rico and Canada, subjects randomised to TNFi arm received adalimumab 40 mg every other week (QOW) by subcutaneous (SC) injection and in all other countries, subjects randomised to TNFi arm received etanercept 50 mg once weekly by SC injection up to 72 months. Subjects were followed up for at least 28 days after last dose of study drug.

Arm type	Active comparator

Investigational medicinal product name	Adalimumab
Investigational medicinal product code	
Other name	Humira
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received adalimumab 40 mg SC QOW.

Investigational medicinal product name	Etanercept
Investigational medicinal product code	
Other name	Enbrel
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received adalimumab 50 mg SC once weekly.

Number of subjects in period 1[1]	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi
Started	1455	1456	1451
Completed	1053	998	1060
Not completed	402	458	391
Consent withdrawn by subject	282	327	289
Death	49	66	38
Unspecified	32	30	24
Lost to follow-up	38	35	40
Global Deterioration of Health Status	1	-	-

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: Baseline analysis was performed on safety analysis set which included all subjects who were randomised in the study and received at least one dose of the randomized investigational drug (tofacitinib or TNFi).

Baseline characteristics

Reporting groups	
Reporting group title	Tofacitinib 5 mg BID
Reporting group description:	
Subjects received tofacitinib 5 milligram (mg) oral tablet twice daily (BID) up to 72 months. Subjects were followed up for at least 28 days after last dose of study drug.	
Reporting group title	Tofacitinib 10 mg BID
Reporting group description:	
Subjects received tofacitinib 10 mg oral tablets (two tablets of 5 mg each) BID up to 72 months. Dose was reduced to tofacitinib 5 mg BID on or after 19 February 2019 as per Study Protocol Amendment 8. Subjects were followed up for at least 28 days after last dose of study drug.	
Reporting group title	TNFi
Reporting group description:	
In the United States (US), Puerto Rico and Canada, subjects randomised to TNFi arm received adalimumab 40 mg every other week (QOW) by subcutaneous (SC) injection and in all other countries, subjects randomised to TNFi arm received etanercept 50 mg once weekly by SC injection up to 72 months. Subjects were followed up for at least 28 days after last dose of study drug.	

Reporting group values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi
Number of subjects	1455	1456	1451
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)	1042	978	989
From 65-84 years	412	477	457
85 years and over	1	1	5
Age Continuous Units: years			
arithmetic mean	60.75	61.40	61.30
standard deviation	± 6.80	± 7.07	± 7.47
Sex: Female, Male Units: subjects			
Female	1169	1124	1117
Male	286	332	334
Race/Ethnicity, Customized Units: Subjects			
White	1128	1126	1099
Black or African American	63	65	83
Asian	65	56	55
Other	199	209	214
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	438	482	470

Not Hispanic or Latino	1017	974	981
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	4362		
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)	3009		
From 65-84 years	1346		
85 years and over	7		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: subjects			
Female	3410		
Male	952		
Race/Ethnicity, Customized Units: Subjects			
White	3353		
Black or African American	211		
Asian	176		
Other	622		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1390		
Not Hispanic or Latino	2972		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	Tofacitinib 5 mg BID

Reporting group description:

Subjects received tofacitinib 5 milligram (mg) oral tablet twice daily (BID) up to 72 months. Subjects were followed up for at least 28 days after last dose of study drug.

Reporting group title	Tofacitinib 10 mg BID

Reporting group description:

Subjects received tofacitinib 10 mg oral tablets (two tablets of 5 mg each) BID up to 72 months. Dose was reduced to tofacitinib 5 mg BID on or after 19 February 2019 as per Study Protocol Amendment 8. Subjects were followed up for at least 28 days after last dose of study drug.

Reporting group title	TNFi

Reporting group description:

In the United States (US), Puerto Rico and Canada, subjects randomised to TNFi arm received adalimumab 40 mg every other week (QOW) by subcutaneous (SC) injection and in all other countries, subjects randomised to TNFi arm received etanercept 50 mg once weekly by SC injection up to 72 months. Subjects were followed up for at least 28 days after last dose of study drug.

Subject analysis set title	All Tofacitinib
Subject analysis set type	Safety analysis

Subject analysis set description:

All participants who received treatment in either tofacitinib 5 mg or tofacitinib 10 mg group BID up to 72 months. Participants were followed up for at least 28 days after last dose of study drug.

Primary: Incidence Rate of Adjudicated Malignancies Excluding Non-melanoma Skin Cancers (NMSC)

End point title	Incidence Rate of Adjudicated Malignancies Excluding Non-melanoma Skin Cancers (NMSC)

End point description:

Incidence rate (number of subjects with event per 100 subject year [SY]) was defined as the total number of subjects with admissible events divided by the total (for all qualifying subjects) time at risk for the cohort/treatment group of interest. Malignancy excluding NMSC were adjudicated by a steering committee. The risk period (RP) was the last contact date. The last contact date was the maximum of (AE start date, AE stop date, last study visit date, withdrawal date, telephone contact date). If a subject died, last contact date was the death date. First events were counted within the RP. If a subject did not have an event or had an event but outside the risk period, the subject was censored at the end of RP. The Safety Analysis Set (SAS) included all subjects who were randomised in the study and received at least one dose of the randomised investigational drug (tofacitinib or TNFi).

End point type	Primary

End point timeframe:

Baseline up to last contact date (maximum up to 72 months)

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	All Tofacitinib
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	1455	1456	1451	2911
Units: subjects with event/100 SY				
number (confidence interval 95%)	1.13 (0.87 to 1.45)	1.13 (0.86 to 1.45)	0.77 (0.55 to 1.04)	1.13 (0.94 to 1.35)

Statistical analyses

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

Secondary comparison. Non-inferiority was to be claimed between tofacitinib 10 mg BID and tofacitinib 5 mg BID if the upper limit of the 95% CI for HR was < 2.0 (non-inferiority criterion).

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	2911
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Hazard ratio (HR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.43

Notes:

[1] - Hazard ratio (95 percent [%] confidence interval [CI]) was based on a univariate cox proportional hazard model with treatment (tofacitinib 5 mg BID, tofacitinib 10 mg BID and TNFi) as covariate.

Statistical analysis title	Tofacitinib 5 mg BID versus TNFi

Statistical analysis description:

Supportive analysis to the primary comparison between All Tofacitinib vs TNFi.

Comparison groups	Tofacitinib 5 mg BID v TNFi
Number of subjects included in analysis	2906
Analysis specification	Pre-specified
Analysis type	other[2]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	2.18

Notes:

[2] - Hazard ratio (95% CI) was based on a univariate cox proportional hazard model with treatment (tofacitinib 5 mg BID, tofacitinib 10 mg BID and TNFi) as covariate.

Statistical analysis title	Tofacitinib 10 mg BID versus TNFi

Statistical analysis description:

Supportive analysis to the primary comparison between All Tofacitinib vs TNFi.

Comparison groups	TNFi v Tofacitinib 10 mg BID
Number of subjects included in analysis	2907
Analysis specification	Pre-specified
Analysis type	other[3]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	2.19

Notes:

[3] - Hazard ratio (95% CI) was based on a univariate cox proportional hazard model with treatment (tofacitinib 5 mg BID, tofacitinib 10 mg BID and TNFi) as covariate.

Statistical analysis title	All Tofacitinib versus TNFi

Statistical analysis description:

Primary comparison. Non-inferiority was to be claimed between All Tofacitinib and TNFi if the upper limit of the 95% CI for HR was < 1.8 (non-inferiority criterion).

Comparison groups	TNFi v All Tofacitinib
Number of subjects included in analysis	4362
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	2.09

Notes:

[4] - Hazard ratio (95% CI) was based on a univariate Cox proportional hazard model with treatment [All Tofacitinib (ie, tofacitinib 5 mg BID and tofacitinib 10 mg BID combined) and TNFi] as covariate.

Primary: Incidence Rate of Adjudicated Major Adverse Cardiovascular Events (MACE)

End point title	Incidence Rate of Adjudicated Major Adverse Cardiovascular Events (MACE)

End point description:

MACE included the cardiovascular death, non-fatal myocardial infarction (MI) and non-fatal stroke of any classification, including reversible focal neurologic defects with imaging evidence of a new cerebral lesion consistent with ischemia or hemorrhage. Incidence rate was defined as the total number of subjects with admissible events divided by the total (for all qualifying subjects) time at risk for the cohort/treatment group of interest. Risk period (RP): minimum of last contact date or last study treatment dose date + 60 days. The last contact date was the maximum of (AE start, AE stop, last study visit, withdrawal, telephone contact date). If a subject died, last contact was the death date. First events were counted within the RP. If a subject did not have an event or had an event but outside the risk period, the subject was censored at the end of RP. SAS included all subjects who were randomised in the study and received at least one dose of the randomised investigational drug.

End point type	Primary

End point timeframe:

Baseline up to last contact date (maximum up to 72 months)

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	All Tofacitinib
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	1455	1456	1451	2911
Units: subjects with event/100 SY				
number (confidence interval 95%)	0.91 (0.67 to 1.21)	1.05 (0.78 to 1.38)	0.73 (0.52 to 1.01)	0.98 (0.79 to 1.19)

Statistical analyses

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Secondary Comparison. Non-inferiority was to be claimed between tofacitinib 10 mg BID and tofacitinib 5 mg BID if the upper limit of the 95% CI for HR was <2.0 (non-inferiority criterion).	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	2911
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.71

Notes:

[5] - Hazard ratio (95% CI) was based on a univariate cox proportional hazard model with treatment (tofacitinib 5 mg BID, tofacitinib 10 mg BID and TNFi) as covariate.

Statistical analysis title	Tofacitinib 5 mg BID versus TNFi
Statistical analysis description:	
Supportive analysis to the primary comparison between All Tofacitinib vs TNFi.	
Comparison groups	Tofacitinib 5 mg BID v TNFi
Number of subjects included in analysis	2906
Analysis specification	Pre-specified
Analysis type	other[6]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.91

Notes:

[6] - Hazard ratio (95% CI) was based on a univariate cox proportional hazard model with treatment (tofacitinib 5 mg BID, tofacitinib 10 mg BID and TNFi) as covariate.

Statistical analysis title	Tofacitinib 10 mg BID versus TNFi
Statistical analysis description:	
Supportive analysis to the primary comparison between All Tofacitinib vs TNFi.	
Comparison groups	Tofacitinib 10 mg BID v TNFi
Number of subjects included in analysis	2907
Analysis specification	Pre-specified
Analysis type	other[7]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	2.18

Notes:

[7] - Hazard ratio (95% CI) was based on a univariate cox proportional hazard model with treatment (tofacitinib 5 mg BID, tofacitinib 10 mg BID and TNFi) as covariate.

Statistical analysis title	All Tofacitinib versus TNFi

Statistical analysis description:

Primary comparison. Non-inferiority was to be claimed between All Tofacitinib and TNFi if the upper limit of the 95% CI for HR was < 1.8 (non-inferiority criterion).

Comparison groups	TNFi v All Tofacitinib
Number of subjects included in analysis	4362
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.94

Notes:

[8] - Hazard ratio (95% CI) was based on a univariate Cox proportional hazard model with treatment [All Tofacitinib (ie, tofacitinib 5 mg BID and tofacitinib 10 mg BID combined) and TNFi] as covariate.

Secondary: Incidence Rate of Non-fatal Stroke

End point title	Incidence Rate of Non-fatal Stroke

End point description:

Non-fatal stroke included reversible focal neurologic defects with imaging evidence of a new cerebral lesion consistent with ischemia or hemorrhage. Incidence rate was defined as the total number of subjects with admissible events divided by the total (for all qualifying subjects) time at risk for the cohort/treatment group of interest. The RP was minimum of last contact date or last study treatment dose date + 60 days. The last contact date was the maximum of (AE start date, AE stop date, last study visit date, withdrawal date, telephone contact date). If a subject died, last contact date was the death date. First events were counted within the RP. If a subject did not have an event or had an event but outside the risk period, the subject was censored at the end of RP. SAS included all subjects who were randomised in the study and received at least one dose of the randomised investigational drug (tofacitinib or TNFi).

End point type	Secondary

End point timeframe:

Baseline up to last contact date (maximum up to 72 months)

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1455	1456	1451	
Units: subjects with event/100 SY				
number (confidence interval 95%)	0.27 (0.15 to 0.45)	0.33 (0.19 to 0.53)	0.34 (0.20 to 0.54)	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence Rate of Non-fatal Myocardial Infarction

End point title	Incidence Rate of Non-fatal Myocardial Infarction

End point description:

Incidence rate was defined as the total number of subjects with admissible events divided by the total (for all qualifying subjects) time at risk for the cohort/treatment group of interest. The RP was minimum of last contact date or last study treatment dose date + 60 days. The last contact date was the maximum of (AE start date, AE stop date, last study visit date, withdrawal date, telephone contact date). If a subject died, last contact date was the death date. First events were counted within the RP. If a subject did not have an event or had an event but outside the risk period, the subject was censored at the end of RP. SAS included all subjects who were randomised in the study and received at least one dose of the randomised investigational drug (tofacitinib or TNFi).

End point type	Secondary

End point timeframe:

Baseline up to last contact date (maximum up to 72 months)

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1455	1456	1451	
Units: subjects with event/100 SY				
number (confidence interval 95%)	0.37 (0.22 to 0.57)	0.33 (0.19 to 0.53)	0.16 (0.07 to 0.31)	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence Rate of Adjudicated Opportunistic Infection Events Including Tuberculosis

End point title	Incidence Rate of Adjudicated Opportunistic Infection Events Including Tuberculosis

End point description:

Opportunistic infections (OI) were reviewed and adjudicated by the opportunistic infection review committee (OIRC). Incidence rate was defined as the total number of subjects with admissible events divided by the total (for all qualifying subjects) time at risk for the cohort/treatment group of interest. The RP was the minimum of last contact date or last study treatment dose date + 28 days. The last contact date was the maximum of (AE start date, AE stop date, last study visit date, withdrawal date, telephone contact date). If a subject died, last contact date was the death date. First events were counted within the RP. If a subject did not have an event or had an event but outside the risk period, the subject was censored at the end of RP. SAS included all subjects who were randomised in the study and received at least one dose of the randomised investigational drug (tofacitinib or TNFi).

End point type	Secondary

End point timeframe:

Baseline up to last contact date (maximum up to 72 months)

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1455	1456	1451	
Units: subjects with event/100 SY				
number (confidence interval 95%)	0.76 (0.54 to 1.04)	0.91 (0.66 to 1.22)	0.42 (0.26 to 0.64)	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence Rate of Adjudicated Hepatic Events

End point title	Incidence Rate of Adjudicated Hepatic Events

End point description:

Hepatic events (adjudicated) included drug-induced liver injury (DILI) - probable, highly likely and definite, DILI – listed separately, DILI – cases meeting classification and severity, subjects with elevations of transaminase levels greater than (>) 1* upper limit of normal (ULN), greater than or equal to (>=) 3*ULN, >=5*ULN (based on laboratory values). Incidence rate was defined as total number of subjects with admissible events divided by total (for all qualifying subjects) time at risk for the cohort/treatment group of interest. RP was minimum of last contact or last study treatment dose date+28 days. Last contact date was maximum of AE start, AE stop, last study visit, withdrawal, telephone contact date. In case of death, last contact was the death date. First events counted within RP. Subject did not have event or had event outside RP were censored at end of RP. SAS included: subjects randomised in study and received at least one dose of the randomised investigational drug.

End point type	Secondary

End point timeframe:

Baseline up to last contact date (maximum up to 72 months)

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1455	1456	1451	
Units: subjects with event/100 SY				
number (confidence interval 95%)	0.90 (0.66 to 1.20)	1.51 (1.18 to 1.91)	0.70 (0.49 to 0.97)	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence Rate of Adjudicated Cardiovascular Events Other Than Major Adverse Cardiovascular Events (MACE)

End point title	Incidence Rate of Adjudicated Cardiovascular Events Other Than Major Adverse Cardiovascular Events (MACE)

End point description:

Cardiovascular events (adjudicated by a Cardiovascular Endpoint Adjudication Committee) included death (coronary and non-coronary), MI, all coronary revascularization, unstable angina, new ischemic heart disease, stroke (fatal and non-fatal), transient ischemic attack, congestive heart failure, peripheral

arterial vascular disease–first diagnosis or procedure, deep vein thrombosis, pulmonary embolism, arterial embolism, arterial thrombosis. Incidence rate: total number of subjects with admissible events divided by total (for all qualifying subjects) time at risk for cohort/treatment group of interest. RP: minimum of last contact or last study treatment dose date +28 days. Last contact date was death date or maximum of dates: AE start, AE stop, last study visit, withdrawal, telephone contact. First events counted within RP. Subject without event or event outside RP were censored at end of RP. SAS: all subjects randomised in study and received at least one dose of drug.

End point type	Secondary

End point timeframe:

Baseline up to last contact date (maximum up to 72 months)

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1455	1456	1451	
Units: subjects with event/100 SY				
number (confidence interval 95%)	1.21 (0.92 to 1.55)	1.45 (1.13 to 1.83)	1.05 (0.78 to 1.38)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects With Treatment Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point description:

AE was any untoward medical occurrence post treatment; event need not necessarily had causal relationship with the treatment or usage. SAE was any untoward medical occurrence at any dose: resulted in death, life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, resulted in congenital anomaly. TEAE was an event that occurred for first time during effective duration of treatment and not seen prior to start of treatment or event seen prior to the start of treatment but increase in severity during treatment. RP for AEs: minimum of last contact date or last study treatment dose + 28 days. RP for SAEs: last contact date. Last contact date was death date or maximum of dates: AE start, AE stop, last study visit, withdrawal, telephone contact. First events counted within RP. SAS: subjects randomised in the study and received at least one dose of randomised drug.

End point type	Secondary

End point timeframe:

AEs: Baseline up to minimum of last contact date or last study treatment dose date+28 days (maximum up to 72 months); SAEs: Baseline up to minimum of last contact date (maximum up to 72 months)

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1455	1456	1451	
Units: subjects				
AEs	1333	1344	1308	
SAEs	373	420	339	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Abnormal Laboratory Parameters

End point title	Number of Subjects With Clinically Significant Abnormal Laboratory Parameters

End point description:

Clinically significant laboratory abnormalities: Hematology: hemoglobin, hematocrit, erythrocytes less than [<] 0.8* lower limit of normal [LLN]), platelets (<0.5* LLN; >1.75* ULN), leukocytes (<0.6*LLN; >1.5*ULN), lymphocytes, neutrophils (<0.8*LLN; >1.2*ULN), eosinophils, monocytes (>1.2*ULN); urinalysis: glucose, protein, hemoglobin, and leukocyte esterase (>=1); chemistry: bilirubin, indirect bilirubin (>1.5*ULN) aspartate aminotransferase, alanine aminotransferase (>3.0*ULN), creatinine, triglycerides, cholesterol (>1.3*ULN) and HDL cholesterol (<0.8*LLN). RP was minimum of last contact date or last study treatment dose date +28 days. Last contact date was (date of death or maximum of dates: AE start, AE stop, last study visit, withdrawal, telephone contact). Subjects without event or event outside RP were censored at end of RP. Analysis population: all subjects in SAS with abnormal baseline and >=1 observation of given laboratory test within RP.

End point type	Secondary

End point timeframe:

Baseline up to last contact date (maximum up to 72 months)

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	919	911	915	
Units: subjects	238	252	167	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence Rate of Adjudicated All-Cause Deaths

End point title	Incidence Rate of Adjudicated All-Cause Deaths

End point description:

All-cause death was defined as the death due to any cause during the course of study. Incidence rate was defined as the total number of subjects with admissible events divided by the total (for all qualifying subjects) time at risk for the cohort/treatment group of interest. Incidence rate of all-cause deaths (adjudicated by Adjudication Committee) was reported in this endpoint. The RP was the minimum of last

contact date or last study treatment dose date + 28 days. The last contact date was the maximum of (AE start date, AE stop date, last study visit date, withdrawal date, telephone contact date). If a subject died, last contact date was the death date. First events were counted within the RP. If a subject did not have an event or had an event but outside the risk period, the subject was censored at the end of RP. SAS included all subjects who were randomised in the study and received at least one dose of the randomised investigational drug (tofacitinib or TNFi).

End point type	Secondary

End point timeframe:

Baseline up to last contact date (maximum up to 72 months)

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1455	1456	1451	
Units: subjects with event/100 SY				
number (confidence interval 95%)				
Deaths-Total	0.50 (0.33 to 0.74)	0.80 (0.57 to 1.09)	0.34 (0.20 to 0.54)	
Deaths-Infections	0.08 (0.02 to 0.20)	0.18 (0.08 to 0.35)	0.06 (0.01 to 0.17)	
Deaths-Cardiovascular Events	0.25 (0.13 to 0.43)	0.41 (0.25 to 0.63)	0.20 (0.10 to 0.36)	
Deaths-Malignancies	0.10 (0.03 to 0.23)	0.00 (0.00 to 0.08)	0.02 (0.00 to 0.11)	
Deaths-Other Causes	0.08 (0.02 to 0.20)	0.21 (0.10 to 0.38)	0.06 (0.01 to 0.17)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Reasons For Permanent or Temporary Discontinuation of Study Medication

End point title	Number of Subjects With Reasons For Permanent or Temporary Discontinuation of Study Medication

End point description:

Number of subjects who permanent or temporary discontinued study medication due to any AE, treatment related AEs, Coronavirus disease 2019 (COVID 19) related AEs, and herpes zoster were reported. The RP was the minimum of last contact date or last study treatment dose date +28 days. The last contact date was maximum of (AE start date, AE stop date, last study visit date, withdrawal date, telephone contact date). If a subject died, last contact date was the death date. First events were counted within the RP. If a subject did not have an event or had an event but outside the risk period, the subject was censored at the end of RP. SAS included all subjects who were randomised in the study and received at least one dose of the randomised investigational drug (tofacitinib or TNFi).

End point type	Secondary

End point timeframe:

Baseline up to last contact date (maximum up to 72 months)

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1455	1456	1451	
Units: subjects				
Permanent discontinuation: AE	210	304	210	
Temporary discontinuation: AEs	665	736	576	
Permanent discontinuation: treatment related AE	111	179	114	
Temporary discontinuation: treatment related AE	407	458	297	
Permanent discontinuation: COVID-19 Related AEs	0	1	0	
Temporary discontinuation: COVID-19 Related AEs	0	1	1	
Permanent discontinuation: Herpes Zoster	6	13	2	
Temporary discontinuation: Herpes Zoster	104	110	33	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Disease Activity Score 28-4 (DAS28-4) C-Reactive Protein (CRP) at Month 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60 and 63

End point title	Change From Baseline in Disease Activity Score 28-4 (DAS28-4) C-Reactive Protein (CRP) at Month 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60 and 63

End point description:

DAS28: disease activity in subjects with rheumatoid arthritis based on 28-joint assessment. DAS28-4(CRP): number of painful joints(TJC28) and swollen joints from 28 joints(SJC28), CRP(milligrams per liter[mg/L]) and PtGA on 100 mm VAS(VAS: score range: 0-100 mm [very well-worst], higher scores=worse condition). DAS28-4(CRP) score range:0-9.4, higher score=more disease activity. DAS28-4(CRP)<=3.2=low disease activity;>3.2 to<=5.1=moderate disease activity;>5.1=high disease activity;<2.6=remission.DAS28-4(CRP)=0.56*square root (sqrt)(TJC28)+0.28*sqrt(SJC28)+0.36*ln(CRP (mg/L)+1)+0.014*PtGA in mm+0.96;ln=natural logarithm. Full Analysis Set(FAS):all randomized subjects and received at least 1 dose. Mixed model for repeated measures(MMRM) used without imputation for missing values. Analyses included data while subjects on treatment and visits with N>50 subject in-group.Number of Subjects Analyzed=number of subjects included in MMRM. Number Analysed=subjects evaluable for each time point.

End point type	Secondary

End point timeframe:

Baseline, Months 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60 and 63

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1409	1391	1386	
Units: units on a scale				
least squares mean (standard error)				

Change at Month 2 (n=1325,1301,1316)	-2.00 (± 0.03)	-2.14 (± 0.03)	-1.89 (± 0.03)	
Change at Month 3 (n=1367, 1328, 1317)	-2.28 (± 0.03)	-2.42 (± 0.03)	-2.19 (± 0.03)	
Change at Month 6 (n=1336, 1298, 1294)	-2.50 (± 0.03)	-2.68 (± 0.03)	-2.40 (± 0.03)	
Change at Month 9 (n=1286, 1246, 1245)	-2.64 (± 0.03)	-2.80 (± 0.03)	-2.54 (± 0.03)	
Change at Month 12 (n=1254, 1204, 1197)	-2.70 (± 0.03)	-2.85 (± 0.03)	-2.60 (± 0.03)	
Change at Month 15 (n=1218, 1171, 1174)	-2.78 (± 0.03)	-2.93 (± 0.03)	-2.67 (± 0.03)	
Change at Month 18 (n=1184, 1121, 1138)	-2.78 (± 0.03)	-2.95 (± 0.03)	-2.76 (± 0.03)	
Change at Month 21 (n=1169, 1076, 1115)	-2.82 (± 0.03)	-2.97 (± 0.03)	-2.76 (± 0.03)	
Change at Month 24 (n=1134, 1051, 1097)	-2.82 (± 0.03)	-2.99 (± 0.03)	-2.77 (± 0.03)	
Change at Month 27 (n=1099, 1015, 1045)	-2.91 (± 0.03)	-3.03 (± 0.03)	-2.81 (± 0.03)	
Change at Month 30 (n=1073, 999, 1039)	-2.92 (± 0.03)	-3.03 (± 0.03)	-2.89 (± 0.03)	
Change at Month 33 (n=1055, 974, 1037)	-2.89 (± 0.03)	-3.03 (± 0.03)	-2.89 (± 0.03)	
Change at Month 36 (n=1029, 951, 1014)	-2.91 (± 0.03)	-2.98 (± 0.03)	-2.88 (± 0.03)	
Change at Month 39 (n=984, 888, 960)	-2.96 (± 0.03)	-2.97 (± 0.03)	-2.91 (± 0.03)	
Change at Month 42 (n=851, 768, 831)	-2.95 (± 0.03)	-3.05 (± 0.03)	-2.93 (± 0.03)	
Change at Month 45 (n=710, 642,673)	-2.94 (± 0.04)	-2.96 (± 0.04)	-2.97 (± 0.04)	
Change at Month 48 (n=567, 506, 537)	-2.98 (± 0.04)	-2.99 (± 0.04)	-2.93 (± 0.04)	
Change at Month 51 (n=458, 419, 414)	-3.00 (± 0.04)	-2.95 (± 0.04)	-2.96 (± 0.04)	
Change at Month 54 (n= 363, 329, 322)	-2.99 (± 0.04)	-3.01 (± 0.05)	-2.99 (± 0.05)	
Change at Month 57 (n= 263, 240, 247)	-2.97 (± 0.05)	-2.93 (± 0.05)	-3.02 (± 0.05)	
Change at Month 60 (n=182, 182, 166)	-3.09 (± 0.06)	-2.94 (± 0.06)	-3.01 (± 0.06)	
Change at Month 63 (n=106. 108, 96)	-3.07 (± 0.08)	-2.99 (± 0.07)	-3.05 (± 0.08)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Simplified Disease Activity Index (SDAI) Score at Month 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60 and 63

End point title	Change From Baseline in Simplified Disease Activity Index (SDAI) Score at Month 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60 and 63

End point description:

SDAI numerical sum of 5 outcome parameters: TJC and SJC both based on a 28-joint assessment, patient’s global assessment of health (PtGA) and physician’s global assessment of health (PhyGA) assessed on 0 to 100 millimeter(mm) VAS (higher scores=greater affection due to disease activity) and CRP(mg/L). SDAI total score ranges: 0 to 86 higher score=greater disease activity. SDAI <=3.3 = disease remission, >3.4 to 11 = low disease activity >11 to 26 =moderate disease activity, and >26 = high disease activity. SDAI = (28TJC)+(28SJC)+PhyGA/10+PtGA/10+CRP/10. FAS: all randomised subjects and received at least one dose of drug. MMRM used without imputation for missing values. Analyses included data while subjects were receiving study drug. Visits with N>50 subjects in treatment group included in analyses. Number of Subjects Analyzed: number of subjects included in mixed model for repeated measures. Number Analysed signifies number of subjects evaluable for each specified time

point.

End point type	Secondary

End point timeframe:

Baseline, Month 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60 and 63

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1378	1356	1346	
Units: units on a scale				
least squares mean (standard error)				
Change at Month 2 (n=1272, 1257, 1258)	-22.95 (± 0.33)	-23.84 (± 0.33)	-22.24 (± 0.33)	
Change at Month 3 (n=1321, 1280, 1273)	-25.73 (± 0.30)	-26.81 (± 0.30)	-25.26 (± 0.30)	
Change at Month 6 (n=1288, 1245, 1244)	-27.63 (± 0.28)	-28.93 (± 0.28)	-27.21 (± 0.28)	
Change at Month 9 (n=1244, 1204, 1197)	-28.81 (± 0.28)	-30.07 (± 0.28)	-28.29 (± 0.28)	
Change at Month 12 (n=1215, 1168, 1143)	-29.56 (± 0.27)	-30.46 (± 0.27)	-28.71 (± 0.27)	
Change at Month 15 (n=1172, 1128, 1129)	-30.20 (± 0.25)	-31.15 (± 0.26)	-29.30 (± 0.26)	
Change at Month 18 (n=1149, 1085, 1092)	-30.14 (± 0.26)	-31.29 (± 0.26)	-30.18 (± 0.26)	
Change at Month 21 (n=1138, 1040, 1072)	-30.42 (± 0.26)	-31.46 (± 0.26)	-30.36 (± 0.26)	
Change at Month 24 (n=1092, 1010, 1051)	-30.51 (± 0.26)	-31.56 (± 0.26)	-30.33 (± 0.26)	
Change at month 27 (n=1056, 979, 1002)	-31.16 (± 0.25)	-31.85 (± 0.26)	-30.53 (± 0.26)	
Change at Month 30 (n=1046, 970, 996)	-31.27 (± 0.25)	-32.02 (± 0.25)	-31.24 (± 0.25)	
Change at Month 33 (n=1027, 947, 997)	-31.06 (± 0.26)	-31.91 (± 0.26)	-31.20 (± 0.26)	
Change at Month 36 (n=994, 917, 978)	-31.26 (± 0.26)	-31.52 (± 0.27)	-31.09 (± 0.26)	
Change at Month 39 (n=954, 857, 920)	-31.77 (± 0.25)	-31.51 (± 0.26)	-31.36 (± 0.26)	
Change at Month 42 (n=819, 733, 800)	-31.62 (± 0.27)	-32.09 (± 0.28)	-31.24 (± 0.27)	
Change at Month 45 (n=692, 617, 646)	-31.27 (± 0.29)	-31.67 (± 0.30)	-31.85 (± 0.30)	
Change at Month 48 (n=547, 485, 522)	-31.87 (± 0.31)	-31.59 (± 0.32)	-31.68 (± 0.32)	
Change at Month 51 (n=438, 406, 400)	-32.15 (± 0.33)	-31.52 (± 0.34)	-31.72 (± 0.34)	
Change at Month 54 (n=347, 316, 314)	-31.91 (± 0.33)	-32.33 (± 0.35)	-31.95 (± 0.35)	
Change at Month 57 (n=253, 235, 242)	-31.58 (± 0.41)	-31.61 (± 0.42)	-31.98 (± 0.42)	
Change at Month 60 (n=174, 179, 161)	-32.84 (± 0.46)	-31.57 (± 0.46)	-32.23 (± 0.48)	
Change at Month 63 (n=102, 107, 95)	-32.27 (± 0.63)	-32.12 (± 0.62)	-32.27 (± 0.66)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Disease Activity Index (CDAI) Score at Month 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60 and 63

End point title	Change From Baseline in Clinical Disease Activity Index (CDAI) Score at Month 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60 and 63

End point description:

CDAI is numerical sum of four outcome parameters: TJC and SJC both based on a 28-joint assessment, PtGA and PhyGA both assessed on 0 to 100 mm VAS (higher scores indicate greater affection due to disease activity). CDAI total score ranges from 0 to 76 with higher score indicating greater disease activity. CDAI <=2.8 indicates disease remission, >2.8 to 10 indicates low disease activity, >10 to 22 indicates moderate disease activity, and >22 indicates high disease activity. CDAI = (28TJC) + (28SJC) + PhyGA/10 + PtGA/10. FAS included all subjects randomized in study and received at least one dose of drug. MMRM was used without imputation for missing values. Analyses included the data while subjects were receiving the study drug. Only visits with N > 50 subjects in each treatment group were included in the analyses. Number of Subjects Analyzed: number of subjects included in MMRM. Number Analyzed 'n' signifies number of subjects evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline, Month 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60 and 63

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1378	1356	1348	
Units: units on a scale				
least squares mean (standard error)				
Change at Month 2 (n=1272, 1258, 1264)	-21.99 (± 0.32)	-22.84 (± 0.32)	-21.30 (± 0.32)	
Change at Month 3 (n=1325, 1281, 1276)	-24.76 (± 0.29)	-25.77 (± 0.29)	-24.29 (± 0.30)	
Change at Month 6 (n=1292, 1246, 1249)	-26.59 (± 0.27)	-27.82 (± 0.28)	-26.21 (± 0.28)	
Change at Month 9 (n=1245, 1207, 1200)	-27.78 (± 0.27)	-29.03 (± 0.27)	-27.30 (± 0.27)	
Change at Month 12 (n=1217, 1169, 1146)	-28.52 (± 0.26)	-29.38 (± 0.26)	-27.73 (± 0.26)	
Change at Month 15 (n=1177, 1129, 1135)	-29.17 (± 0.25)	-30.06 (± 0.25)	-28.38 (± 0.25)	
Change at Month 18 (n=1152, 1086, 1096)	-29.12 (± 0.25)	-30.21 (± 0.26)	-29.15 (± 0.25)	
Change at Month 21 (n=1141, 1041, 1075)	-29.45 (± 0.25)	-30.49 (± 0.26)	-29.40 (± 0.25)	
Change at Month 24 (n=1093, 1013, 1055)	-29.54 (± 0.25)	-30.49 (± 0.26)	-29.39 (± 0.25)	

Change at Month 27 (n=1058 , 979, 1011)	-30.16 (± 0.24)	-30.82 (± 0.25)	-29.54 (± 0.25)	
Change at Month 30 (n=1049, 970, 1002)	-30.27 (± 0.24)	-30.99 (± 0.25)	-30.24 (± 0.25)	
Change at Month 33 (n=1034, 951, 1000)	-30.05 (± 0.25)	-30.85 (± 0.25)	-30.23 (± 0.25)	
Change at Month 36 (n=999, 920, 982)	-30.29 (± 0.25)	-30.50 (± 0.26)	-30.14 (± 0.25)	
Change at Month 39 (n=958, 858, 923)	-30.78 (± 0.24)	-30.49 (± 0.25)	-30.35 (± 0.25)	
Change at Month 42 (n=820, 736, 801)	-30.66 (± 0.26)	-31.05 (± 0.27)	-30.25 (± 0.26)	
Change at Month 45 (n=694, 618, 650)	-30.28 (± 0.28)	-30.68 (± 0.29)	-30.83 (± 0.29)	
Change at Month 48 (n=547, 487, 522)	-30.85 (± 0.30)	-30.57 (± 0.32)	-30.69 (± 0.31)	
Change at Month 51 (n=440, 407, 401)	-31.09 (± 0.32)	-30.50 (± 0.33)	-30.74 (± 0.33)	
Change at Month 54 (n=347, 317, 314)	-31.03 (± 0.32)	-31.38 (± 0.33)	-31.02 (± 0.33)	
Change at Month 57 (n=254, 236, 242)	-30.62 (± 0.40)	-30.75 (± 0.41)	-30.95 (± 0.41)	
Change at Month 60 (n=175, 179, 161)	-31.74 (± 0.45)	-30.57 (± 0.45)	-31.31 (± 0.47)	
Change at Month 63 (n=102, 107, 95)	-31.23 (± 0.58)	-31.08 (± 0.57)	-31.65 (± 0.60)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved Observed American College of Rheumatology-European League Against Rheumatism (ACR-EULAR) Boolean Remission Criteria

End point title	Percentage of Subjects Who Achieved Observed American College of Rheumatology-European League Against Rheumatism (ACR-EULAR) Boolean Remission Criteria

End point description:

ACR-EULAR Boolean-based definition of remission subject must satisfy all of the following: TJC28 <=1, SJC28 <=1, CRP <=10 mg/L, PtGA on a 0-100 mm scale, higher scores indicate greater affection due to disease activity. FAS included all subjects who were randomised in the study and received at least one dose of the randomised investigational drug (tofacitinib or TNFi). Analyses included the data while the subjects were receiving the study drug. Here, Number Analysed 'n' signifies number of subjects evaluable for each specified time point. Last observation carried forward (LOCF) was applied for missing components, and then composite binary endpoint was calculated. The percentages were calculated using the numbers of subjects evaluable at each visit as the denominators.

End point type	Secondary

End point timeframe:

Month 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69 and 72

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1455	1456	1451	
Units: percentage of subjects				
number (not applicable)				
Month 2 (n=1356, 1342, 1368)	3.83	4.99	3.22	
Month 3 (n=1432, 1424, 1427)	5.73	7.72	6.10	
Month 6 (n=1417, 1398, 1411)	9.10	10.66	7.80	
Month 9 (n=1392, 1349, 1384)	10.85	12.60	8.96	
Month 12 (n=1372, 1332, 1360)	11.22	13.06	9.12	
Month 15 (n=1353, 1311, 1342)	12.56	15.18	10.28	
Month 18 (n=1322, 1284, 1316)	12.10	16.04	11.78	
Month 21 (n=1302, 1255, 1294)	12.90	15.22	13.45	
Month 24 (n=1287, 1226, 1273)	13.60	15.99	13.35	
Month 27 (n=1269, 1211, 1255)	13.24	17.59	14.82	
Month 30 (n=1248, 1191, 1237)	13.46	16.96	14.31	
Month 33 (n=1232, 1177, 1221)	13.88	15.97	14.82	
Month 36 (n=1206, 1162, 1211)	14.51	16.18	14.53	
Month 39 (n=1183, 1140, 1201)	13.78	14.30	15.15	
Month 42 (n=1163, 1110, 1179)	14.79	15.41	15.01	
Month 45 (n=1021, 970, 1023)	14.89	15.46	15.74	
Month 48 (n=865, 806, 839)	15.14	13.90	17.28	
Month 51 (n=698, 671, 689)	14.33	15.50	16.26	
Month 54 (n=564, 548, 550)	14.01	16.42	16.36	
Month 57 (n=444, 445, 431)	15.54	14.16	15.08	
Month 60 (n=327, 330, 321)	11.31	12.73	15.58	
Month 63 (n=221, 230, 223)	11.76	16.96	15.25	
Month 66 (n=122, 131, 122)	9.02	16.79	13.11	
Month 69 (n=46, 46, 48)	13.04	19.57	14.58	
Month 72 (n=12, 18, 15)	8.33	22.22	13.33	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Simplified Disease Activity Index (SDAI) Less Than or Equal to (<=) 3.3

End point title	Percentage of Subjects With Simplified Disease Activity Index (SDAI) Less Than or Equal to (<=) 3.3

End point description:

SDAI is numerical sum of five outcome parameters: TJC and SJC both based on a 28-joint assessment, PtGA and PhyGA both assessed on a 0 to 100 mm VAS (higher scores = greater affection due to disease activity), and CRP (mg/L). SDAI total score ranges from 0 to 86 with higher score indicating greater disease activity. SDAI <=3.3 indicates disease remission, >3.4 to 11 = low disease activity >11 to 26 = moderate disease activity, and >26 = high disease activity. SDAI = (28TJC) + (28SJC) + PhyGA/10+ PtGA/10 + CRP/10. FAS: all subjects randomised in the study and received at least one dose of randomised investigational drug. Analyses included the data while the subjects receiving the study drug. Here, Number Analysed 'n' signifies number of subjects evaluable for each specified time point. LOCF was applied for missing components, and then composite binary endpoint was calculated.

End point type	Secondary

End point timeframe:

Month 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69 and 72

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1455	1456	1451	
Units: percentage of subjects				
number (not applicable)				
Month 2 (n=1320, 1308, 1325)	4.62	7.03	4.15	
Month 3 (n=1425, 1409, 1416)	9.19	11.14	7.84	
Month 6 (n=1414, 1391, 1404)	12.38	14.23	10.40	
Month 9 (n=1390, 1349, 1380)	15.90	17.72	12.75	
Month 12 (n=1372, 1332, 1358)	15.89	18.69	13.92	
Month 15 (n=1353, 1311, 1340)	18.26	20.29	15.90	
Month 18 (n=1322, 1284, 1316)	18.68	21.96	16.79	
Month 21 (n=1302, 1255, 1294)	20.89	22.07	17.93	
Month 24 (n=1287, 1226, 1273)	20.44	22.76	18.93	
Month 27 (n=1269, 1211, 1255)	21.91	23.62	21.12	
Month 30 (n=1248, 1191, 1237)	21.31	23.68	21.91	
Month 33 (n=1232, 1177, 1221)	21.43	25.06	22.19	
Month 36 (n=1206, 1162, 1211)	22.47	24.35	21.80	
Month 39 (n=1183, 1140, 1201)	22.99	24.21	21.48	
Month 42 (n=1163, 1110, 1179)	24.59	24.23	23.41	
Month 45 (n=1021, 970, 1023)	25.27	23.20	23.26	
Month 48 (n=865, 806, 839)	25.32	23.20	24.20	
Month 51 (n=698, 671, 689)	23.35	23.85	24.24	
Month 54 (n=564, 548, 550)	22.34	24.09	24.55	
Month 57 (n=444, 445, 431)	24.10	23.82	24.83	
Month 60 (n=327, 330, 321)	18.65	20.30	25.23	
Month 63 (n=221, 230, 223)	19.00	23.48	23.32	
Month 66 (n=122, 131, 122)	14.75	21.37	20.49	
Month 69 (n=46, 46, 48)	17.39	17.39	22.92	
Month 72 (n=12, 8, 15)	16.67	22.22	13.33	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Disease Activity Index (CDAI) <=2.8

End point title	Percentage of Subjects With Clinical Disease Activity Index (CDAI) <=2.8

End point description:

CDAI is numerical sum of four outcome parameters: TJC and SJC both based on a 28-joint assessment, PtGA and PhyGA assessed on a 0 to 100 mm VAS (higher scores indicate greater affection due to disease activity). CDAI total score ranges from 0 to 76 with higher score = greater disease activity. CDAI <=2.8 = disease remission, >2.8 to 10 = low disease activity, >10 to 22 = moderate disease

activity, >22 = high disease activity. CDAI = (28TJC) + (28SJC) + PhyGA/10 + PtGA/10. FAS: all subjects randomised in the study and received at least one dose of the randomised investigational drug. Analyses included the data while subjects were receiving the study drug. Here, Number Analysed signifies number of subjects evaluable for each specified time point. LOCF was applied for missing components, and then composite binary endpoint was calculated. The percentages were calculated using the numbers of subjects evaluable at each visit as the denominators.

End point type	Secondary

End point timeframe:

Month 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69 and 72

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1455	1456	1451	
Units: percentage of subjects				
number (not applicable)				
Month 2 (n=1320, 1311, 1330)	4.70	7.40	4.36	
Month 3 (n=1425, 1410, 1417)	9.26	11.06	7.76	
Month 6 (n=1414, 1391, 1405)	12.87	14.31	10.32	
Month 9 (n=1390, 1349, 1381)	15.76	18.09	13.25	
Month 12 (n=1372, 1332, 1359)	16.33	18.62	14.64	
Month 15 (n=1353, 1311, 1341)	18.03	21.36	16.41	
Month 18 (n=1322, 1284, 1316)	19.82	22.12	17.93	
Month 21 (n=1302, 1255, 1294)	21.35	22.55	18.70	
Month 24 (n=1287, 1226, 1273)	20.44	22.76	19.48	
Month 27 (n=1269, 1211, 1255)	22.77	23.29	21.51	
Month 30 (n=1248, 1191, 1237)	21.88	24.18	22.31	
Month 33 (n=1232, 1177, 1221)	22.24	25.91	22.36	
Month 36 (n=1206, 1162, 1211)	23.22	25.30	21.64	
Month 39 (n=1183, 1140, 1201)	23.92	24.30	21.90	
Month 42 (n=1163, 1110, 1179)	25.02	24.95	23.66	
Month 45 (n=1021, 970, 1023)	25.95	24.23	23.85	
Month 48 (n=865, 806, 839)	25.55	24.44	24.31	
Month 51 (n=698, 671, 689)	24.50	24.89	25.11	
Month 54 (n=564, 548, 550)	23.23	25.00	25.45	
Month 57 (n=444, 445, 431)	24.32	24.04	25.75	
Month 60 (n=327, 330, 321)	19.88	20.91	26.48	
Month 63 (n=221, 230, 223)	20.81	22.17	22.87	
Month 66 (n=122, 131, 122)	13.93	22.14	17.21	
Month 69 (n=46, 46, 48)	19.57	19.57	18.75	
Month 72 (n=12, 18, 15)	16.67	22.22	13.33	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Simplified Disease Activity Index (SDAI) <=11

End point title	Percentage of Subjects With Simplified Disease Activity Index (SDAI) <=11

End point description:

SDAI is numerical sum of five outcome parameters: TJC and SJC both based on a 28-joint assessment, PtGA and PGA both assessed on a 0 to 100 mm VAS (higher scores indicate greater affection due to disease activity), and CRP (mg/L). SDAI total score ranges from 0 to 86 with higher score indicating greater disease activity. SDAI <=3.3 = disease remission, >3.4 to 11 = disease activity >11 to 26 = moderate disease activity, and >26 = high disease activity. SDAI = (28TJC) + (28SJC) + PhyGA/10 + PtGA/10 + CRP/10. FAS: all subjects randomised in the study and received at least one dose of the randomised investigational drug. Analyses included the data while the subjects were receiving the study drug. Number Analysed signifies number of subjects evaluable for each specified time point. LOCF was applied for missing components, and then composite binary endpoint was calculated. The percentages were calculated using the numbers of subjects evaluable at each visit as the denominators.

End point type	Secondary

End point timeframe:

Month 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69 and 72

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1455	1456	1451	
Units: percentage of subjects				
number (not applicable)				
Month 2 (n=1320, 1308, 1325)	30.76	35.02	28.08	
Month 3 (n=1425, 1409, 1416)	41.47	45.00	37.99	
Month 6 (n=1414, 1391, 1404)	50.85	53.56	45.80	
Month 9 (n=1390, 1349, 1380)	56.40	59.82	52.90	
Month 12 (n=1372, 1332, 1358)	57.87	61.11	54.93	
Month 15 (n=1353, 1311, 1340)	61.12	63.92	57.39	
Month 18 (n=1322, 1284, 1316)	62.10	65.19	60.41	
Month 21 (n=1302, 1255, 1294)	62.75	65.26	61.21	
Month 24 (n=1287, 1226, 1273)	63.17	66.15	61.59	
Month 27 (n=1269, 1211, 1255)	65.17	66.97	63.67	
Month 30 (n=1248, 1191, 1237)	67.23	68.35	65.64	
Month 33 (n=1232, 1177, 1221)	65.75	68.82	65.36	
Month 36 (n=1206, 1162, 1211)	67.33	66.61	65.48	
Month 39 (n=1183, 1140, 1201)	69.74	67.11	66.03	
Month 42 (n=1163, 1110, 1179)	68.96	70.72	66.41	
Month 45 (n=1021, 970, 1023)	68.36	68.97	67.55	
Month 48 (n=865, 806, 839)	67.28	64.76	67.94	
Month 51 (n=698, 671, 689)	67.91	67.51	67.78	
Month 54 (n=564, 548, 550)	64.89	68.61	68.00	
Month 57 (n=444, 445, 431)	63.51	66.29	68.21	
Month 60 (n=327, 330, 321)	63.30	66.67	64.17	
Month 63 (n=221, 230, 223)	61.54	68.26	64.57	
Month 66 (n=122, 131, 122)	59.02	71.76	59.02	
Month 69 (n=46, 46, 48)	60.87	65.22	68.75	
Month 72 (n=12, 18, 15)	50.00	66.67	60.00	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Disease Activity Index (CDAI) <=10

End point title	Percentage of Subjects With Clinical Disease Activity Index (CDAI) <=10

End point description:

CDAI is numerical sum of four outcome parameters: TJC and SJC both based on a 28-joint assessment, PtGA and PhyGA assessed on a 0 to 100 mm VAS (higher scores indicate greater affection due to disease activity). CDAI total score ranges from 0 to 76 with higher score = greater disease activity. CDAI <=2.8 = disease remission, >2.8 to 10 = low disease activity, >10 to 22 = moderate disease activity, >22 = high disease activity. CDAI = (28TJC) + (28SJC) + PhyGA/10 + PtGA/10. FAS: all subjects randomised in the study and received at least one dose of the randomised investigational drug. Analyses included the data while subjects were receiving the study drug. Here, Number Analysed signifies number of subjects evaluable for each specified time point. LOCF was applied for missing components, and then composite binary endpoint was calculated. The percentages were calculated using the numbers of subjects evaluable at each visit as the denominators.

End point type	Secondary

End point timeframe:

Month 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69 and 72

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1455	1456	1451	
Units: percentage of subjects				
number (not applicable)				
Month 2 (n=1320, 1311, 1330)	29.47	34.25	26.92	
Month 3 (n=1425, 1410, 1417)	40.07	43.90	35.99	
Month 6 (n=1414, 1391, 1405)	49.36	51.83	43.63	
Month 9 (n=1390, 1349, 1381)	55.40	58.78	50.91	
Month 12 (n=1372, 1332, 1359)	56.56	59.38	53.57	
Month 15 (n=1353, 1311, 1341)	60.31	62.70	55.93	
Month 18 (n=1322, 1284, 1316)	60.51	64.02	59.42	
Month 21 (n=1302, 1255, 1294)	61.37	64.94	60.20	
Month 24 (n=1287, 1226, 1273)	62.78	65.25	61.19	
Month 27 (n=1269, 1211, 1255)	64.93	66.39	62.87	
Month 30 (n=1248, 1191, 1237)	67.15	67.84	65.00	
Month 33 (n=1232, 1177, 1221)	65.50	67.71	65.03	
Month 36 (n=1206, 1162, 1211)	66.67	65.15	64.66	
Month 39 (n=1183, 1140, 1201)	68.64	66.40	65.61	
Month 42 (n=1163, 1110, 1179)	68.44	69.10	65.82	
Month 45 (n=1021, 970, 1023)	67.97	68.66	67.16	
Month 48 (n=865, 806, 839)	66.71	63.15	67.58	
Month 51 (n=698, 671, 689)	67.77	65.87	67.63	
Month 54 (n=564, 548, 550)	64.54	67.88	68.00	
Month 57 (n=444, 445, 431)	62.61	65.39	67.98	
Month 60 (n=327, 330, 321)	63.00	65.15	65.42	
Month 63 (n=221, 230, 223)	62.90	66.52	66.37	
Month 66 (n=122, 131, 122)	57.38	67.94	61.48	

Month 69 (n=46, 46, 48)	58.70	65.22	66.67	
Month 72 (n=12, 18, 15)	50.00	66.67	53.33	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Disease Activity Score 28-4 (DAS28-4) C-reactive Protein (CRP) <=3.2

End point title	Percentage of Subjects With Disease Activity Score 28-4 (DAS28-4) C-reactive Protein (CRP) <=3.2

End point description:

DAS28: measure of disease activity in subjects with rheumatoid arthritis based on 28-joint assessment. DAS28-4 (CRP): calculated from number of painful joints (TJC28) and swollen joints out of 28 joints (SJC28), CRP (mg/L) and PtGA on 100 mm VAS (VAS: score range: 0-100 mm [very well-worst], higher scores=worse condition). DAS28-4 (CRP) score range: 0-9.4, higher score=more disease activity. DAS28-4 (CRP) <= 3.2 = low disease activity; > 3.2 to <=5.1 = moderate disease activity; >5.1 = high disease activity, and < 2.6 = remission. DAS28-4 (CRP) = 0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) + 0.36*ln(CRP (mg/L) + 1) + 0.014*PtGA in mm + 0.96. Analysis performed on FAS. Analyses included the data while subjects receiving the drug. Number Analysed signifies number of subjects evaluable for each specified time point. LOCF applied for missing components then composite binary endpoint was calculated. The percentages were calculated using number of subjects evaluable at each visit as denominator.

End point type	Secondary

End point timeframe:

Month 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69 and 72

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1455	1456	1451	
Units: percentage of subjects				
number (not applicable)				
Month 2 (n=1347, 1327, 1354)	31.55	35.57	28.36	
Month 3 (n=1430, 1418, 1420)	41.68	46.05	37.54	
Month 6 (n=1416, 1396, 1406)	50.28	54.87	44.88	
Month 9 (n=1392, 1349, 1381)	56.11	59.01	50.91	
Month 12 (n=1372, 1332, 1359)	57.73	60.06	53.05	
Month 15 (n=1353, 1311, 1341)	60.38	63.54	55.03	
Month 18 (n=1322, 1284, 1316)	61.72	63.86	58.51	
Month 21 (n=1302, 1255, 1294)	62.29	63.67	59.27	
Month 24 (n=1287, 1226, 1273)	61.93	64.11	59.78	
Month 27 (n=1269, 1211, 1255)	64.22	67.63	60.56	
Month 30 (n=1248, 1191, 1237)	64.66	65.49	63.22	
Month 33 (n=1232, 1177, 1221)	63.80	66.02	62.82	
Month 36 (n=1206, 1162, 1211)	64.43	64.63	62.59	
Month 39 (n=1183, 1140, 1201)	65.85	65.18	63.53	
Month 42 (n=1163, 1110, 1179)	65.43	67.93	65.31	
Month 45 (n=1021, 970, 1023)	64.74	65.77	64.52	

Month 48 (n=865, 806, 839)	64.39	64.52	64.36	
Month 51 (n=698, 671, 689)	65.19	66.47	65.46	
Month 54 (n=564, 548, 550)	64.18	66.24	66.55	
Month 57 (n=444, 445, 431)	63.06	63.60	67.29	
Month 60 (n=327, 330, 321)	62.69	64.24	65.11	
Month 63 (n=221, 230, 223)	60.18	64.35	68.61	
Month 66 (n=122, 131, 122)	55.74	66.41	60.66	
Month 69 (n=46, 46, 48)	58.70	56.52	70.83	
Month 72 (n=12, 18, 15)	50.00	61.11	73.33	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With an American College of Rheumatology 20 Percent (%) (ACR20) Response

End point title	Number of Subjects With an American College of Rheumatology 20 Percent (%) (ACR20) Response

End point description:

ACR20 response: >=20% improvement in TJC (28) and SJC (28) and >=20% improvement in 3 of 5 remaining ACR-core criteria:1)PGA arthritis,2)PtGA arthritis,3)Subject’s assessment arthritis pain,4)subject’s assessment functional disability by HAQ-DI,and 5)CRP (mg/L) at each visit. PGA: physician's global assessment of arthritis on VAS, 0(very well) to 100mm(worst arthritis), higher scores=worse condition. PtGA:subject’s global assessment of arthritis on VAS, 0(very well) to 100 mm(worst arthritis condition), higher scores=worse condition. Subject’s assessment of arthritis pain: assessed on VAS, 0(no pain) to 100mm(most severe pain), higher score=more pain. HAQ-DI: functional disability evaluation, score:0 (no difficulty) to 3(unable to do), higher score=more disability. Analysis performed on FAS and included data while subjects were receiving drug. Number Analysed 'n'=subjects evaluable for each time point. LOCF applied for missing components then composite binary endpoint

End point type	Secondary

End point timeframe:

Month 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69 and 72

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1455	1456	1451	
Units: subjects				
Month 2 (n=1335, 1316, 1337)	832	867	812	
Month 3 (n=1418, 1398, 1396)	979	992	923	
Month 6 (n=1402, 1375, 1382)	999	1012	981	
Month 9 (n=1375, 1328, 1356)	1019	1004	987	
Month 12 (n=1362, 1308, 1333)	1033	992	966	
Month 15 (n=1341, 1291, 1315)	1017	1003	969	
Month 18 (n=1309, 1266, 1289)	981	974	937	
Month 21 (n=1289, 1238, 1271)	955	953	949	
Month 24 (n=1275, 1209, 1251)	956	922	922	
Month 27 (n=1255, 1190, 1234)	961	917	913	
Month 30 (n=1237, 1173, 1213)	932	899	931	
Month 33 (n=1220, 1157, 1194)	935	888	922	

Month 36 (n=1193, 1145, 1189)	907	881	887	
Month 39 (n=1172,1122, 1180)	896	843	887	
Month 42 (n=1153, 1091, 1154)	905	848	883	
Month 45 (n=1010, 955, 1006)	780	718	790	
Month 48 (n=854, 795, 821)	654	587	639	
Month 51 (n=691, 659, 675)	535	485	518	
Month 54 (n=559, 536, 538)	434	396	400	
Month 57 (n=441, 436, 421)	337	321	302	
Month 60 (n=323, 323, 314)	243	237	232	
Month 63 (n=217, 221, 220)	163	166	161	
Month 66 (n=119, 130, 122)	85	101	89	
Month 69 (n=46, 46, 48)	26	36	37	
Month 72 (n=11, 18, 15)	5	15	10	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With an American College of Rheumatology 50% (ACR50) Response

End point title	Number of Subjects With an American College of Rheumatology 50% (ACR50) Response

End point description:

ACR50 response is >=50% improvement in TJC (28) and SJC (28) and >=50% improvement in 3 of 5 remaining ACR-core criteria:1)PGA arthritis,2)PtGA arthritis,3)Subject’s assessment arthritis pain, 4)Subject’s assessment functional disability by HAQ-DI,and 5)CRP (mg/L) at each visit. PGA: physician's global assessment of arthritis on VAS, 0(very well) to100mm(worst arthritis), higher scores=worse condition. PtGA: subject assessed health on VAS, 0(very well) to 100mm(worst arthritis condition), higher scores=worse condition. Subject’s assessment of arthritis pain: assessed on VAS, 0 mm (no pain) to 100 mm (most severe pain), higher score=more pain. HAQ-DI: functional disability evaluation, score:0(no difficulty) to 3(unable to do), higher score=more disability. Analysis performed on FAS and included data while subjects receiving study drug. Number Analysed 'n'= subjects evaluable for each specified time point. LOCF applied for missing components then composite binary endpoint calculated.

End point type	Secondary

End point timeframe:

Month 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69 and 72

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1455	1456	1451	
Units: subjects				
Month 2 (n=1337, 1321, 1346)	402	452	336	
Month 3 (n=1422, 1405, 1404)	528	561	460	
Month 6 (n=1408, 1378, 1387)	605	614	533	
Month 9 (n=1381, 1333, 1356)	620	651	577	
Month 12 (n=1362, 1312, 1334)	631	654	577	
Month 15 (n=1340, 1290, 1313)	652	668	582	
Month 18 (n=1312, 1265, 1290)	633	643	609	
Month 21 (n=1290, 1234, 1272)	607	623	608	

Month 24 (n=1276, 1209, 1249)	622	616	592	
Month 27 (n=1258, 1194, 1231)	620	602	596	
Month 30 (n=1236, 1177, 1213)	599	609	610	
Month 33 (n=1220, 1158, 1200)	585	611	594	
Month 36 (n=1195, 1143, 1188)	603	566	592	
Month 39 (n=1170, 1121, 1179)	595	588	561	
Month 42 (n=1151, 1093, 1161)	592	578	587	
Month 45 (n=1011, 955, 1008)	521	481	519	
Month 48 (n=854, 794, 826)	422	385	424	
Month 51 (n=693, 659, 677)	350	320	346	
Month 54 (n=560, 538, 540)	284	271	268	
Month 57 (n=440, 437, 422)	200	210	209	
Month 60 (n=325, 322, 314)	152	151	150	
Month 63 (n=220, 223, 219)	100	104	103	
Month 66 (n=122, 129, 121)	52	68	55	
Month 69 (n=45, 45, 47)	16	20	27	
Month 72 (n=11, 18, 15)	3	6	7	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With an American College of Rheumatology 70% (ACR70) Response

End point title	Number of Subjects With an American College of Rheumatology 70% (ACR70) Response

End point description:

ACR70 response is >= 70% improvement in TJC (28) and SJC (28) and >=70% improvement in 3 of 5 remaining ACR-core criteria: 1)PGA arthritis, 2)PtGA arthritis, 3) Subject’s assessment arthritis pain, 4)Subject’s assessment of functional disability by HAQ-DI, and 5)CRP (mg/L) at each visit. PGA: physician's global assessment on VAS, 0(very well) to 100 mm(worst arthritis), higher scores=worse condition. PtGA: Subject’s global assessment on VAS, 0(very well) to100mm(worst arthritis condition), higher scores=worse condition. Subject’s assessment of arthritis pain: assessed on VAS, 0 (no pain) to 100 mm (most severe pain), higher score=more pain. HAQ-DI: functional disability evaluation, score: 0 (no difficulty) to 3 (unable to do), higher score=more disability. Analysis performed on FAS and included data while subjects receiving study drug. Number Analysed 'n'= subjects evaluable for each time point. LOCF applied for missing components then composite binary endpoint calculated.

End point type	Secondary

End point timeframe:

Month 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69 and 72

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1455	1456	1451	
Units: subjects				
Month 2 (n=1343, 1326, 1354)	152	193	113	
Month 3 (n=1425, 1414, 1413)	253	268	199	
Month 6 (n=1409, 1388, 1397)	282	331	234	
Month 9 (n=1383, 1336, 1366)	328	367	291	

Month 12 (n=1364, 1312, 1338)	337	373	284	
Month 15 (n=1342, 1294, 1323)	359	390	304	
Month 18 (n=1311, 1269, 1295)	358	382	325	
Month 21 (n=1293, 1238, 1277)	362	370	322	
Month 24 (n=1279, 1211, 1255)	349	386	328	
Month 27 (n=1259, 1192, 1238)	374	390	342	
Month 30 (n=1238, 1177, 1221)	369	397	358	
Month 33 (n=1222, 1160, 1204)	357	392	355	
Month 36 (n=1195, 1145, 1193)	362	343	351	
Month 39 (n=1173, 1125, 1186)	371	361	338	
Month 42 (n=1152, 1098, 1163)	376	342	343	
Month 45 (n=1010, 957, 1006)	313	298	298	
Month 48 (n=855, 794, 826)	256	228	238	
Month 51 (n=691, 657, 677)	216	195	199	
Month 54 (n=559, 538, 538)	159	163	160	
Month 57 (n=441, 438, 421)	128	127	118	
Month 60 (n=326, 321, 315)	79	83	92	
Month 63 (n=220, 223, 219)	58	57	64	
Month 66 (n=122, 130, 122)	25	38	35	
Month 69 (n=46, 45, 48)	8	15	14	
Month 72 (n=11, 18, 15)	2	5	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) at Months 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60 and 63

End point title	Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) at Months 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60 and 63

End point description:

HAQ-DI: degree of difficulty subject experienced during past week in 8 domains of daily living activities: dressing/grooming; arising; eating; walking; reach; grip; hygiene; and other activities. Total of 30 items distributed in 8 domains. Each item scored on 4-point scale from 0 to 3: 0=no difficulty; 1=some difficulty; 2=much difficulty; 3=unable to do. Overall score computed as sum of domain scores and divided by number of domains answered. Total possible score range 0 (least difficulty) and 3 (extreme difficulty), higher scores =more difficulty while performing daily living activities. FAS: all randomised subjects and received at least 1 dose of drug. MMRM used without imputation for missing values. Analyses included data while subjects were receiving drug. Visits with N>50 subjects in group included in analyses. Number of Subjects Analyzed" is number of subjects included in MMRM. Number Analysed= signifies number of subjects evaluable for each time point.

End point type	Secondary

End point timeframe:

Baseline, Months 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60 and 63

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1409	1390	1388	
Units: units on a scale				
least squares mean (standard error)				
Change at Month 2 (n=1325, 1301, 1323)	-0.42 (± 0.02)	-0.45 (± 0.02)	-0.38 (± 0.02)	
Change at Month 3 (n=1371, 1329, 1320)	-0.45 (± 0.02)	-0.48 (± 0.02)	-0.42 (± 0.02)	
Change at Month 6 (n=1341, 1297, 1299)	-0.50 (± 0.02)	-0.51 (± 0.02)	-0.46 (± 0.02)	
Change at Month 9 (n=1287, 1247, 1248)	-0.51 (± 0.02)	-0.55 (± 0.02)	-0.47 (± 0.02)	
Change at Month 12 (n=1256, 1205, 1200)	-0.52 (± 0.02)	-0.53 (± 0.02)	-0.49 (± 0.02)	
Change at Month 15 (n=1223, 1171, 1179)	-0.53 (± 0.02)	-0.56 (± 0.02)	-0.51 (± 0.02)	
Change at Month 18 (n=1189, 1122, 1143)	-0.52 (± 0.02)	-0.56 (± 0.02)	-0.49 (± 0.02)	
Change at Month 21 (n=1172, 1076, 1118)	-0.53 (± 0.02)	-0.55 (± 0.02)	-0.50 (± 0.02)	
Change at Month 24 (n=1135, 1052, 1101)	-0.52 (± 0.02)	-0.57 (± 0.02)	-0.49 (± 0.02)	
Change at Month 27 (n=1102, 1015, 1054)	-0.52 (± 0.02)	-0.56 (± 0.02)	-0.51 (± 0.02)	
Change at Month 30 (n=1078, 998, 1045)	-0.53 (± 0.02)	-0.55 (± 0.02)	-0.50 (± 0.02)	
Change at Month 33 (n=1063, 977, 1041)	-0.51 (± 0.02)	-0.56 (± 0.02)	-0.52 (± 0.02)	
Change at Month 36 (n=1034, 953, 1020)	-0.50 (± 0.02)	-0.54 (± 0.02)	-0.48 (± 0.02)	
Change at Month 39 (n=989, 892, 964)	-0.51 (± 0.02)	-0.54 (± 0.02)	-0.49 (± 0.02)	
Change at Month 42 (n=854, 770, 833)	-0.51 (± 0.02)	-0.52 (± 0.02)	-0.50 (± 0.02)	
Change at Month 45 (n=713, 642, 678)	-0.50 (± 0.02)	-0.51 (± 0.02)	-0.51 (± 0.02)	
Change at Month 48 (n=569, 509, 539)	-0.50 (± 0.02)	-0.50 (± 0.02)	-0.48 (± 0.02)	
Change at Month 51 (n=461, 420, 416)	-0.53 (± 0.02)	-0.49 (± 0.02)	-0.50 (± 0.02)	
Change at Month 54 (n=364, 330, 324)	-0.53 (± 0.02)	-0.51 (± 0.02)	-0.48 (± 0.02)	
Change at Month 57 (n=266, 240, 247)	-0.49 (± 0.02)	-0.48 (± 0.02)	-0.48 (± 0.02)	
Change at Month 60 (n=185, 181, 167)	-0.52 (± 0.03)	-0.49 (± 0.03)	-0.48 (± 0.03)	
Change at Month 63 (n=107, 108, 96)	-0.54 (± 0.03)	-0.48 (± 0.03)	-0.48 (± 0.04)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to last contact date (maximum up to 72 months)

Adverse event reporting additional description:

Same event may appear as both AE and SAE. What is presented are distinct events. An event may categorized as serious in 1 subject and non-serious in another, or subject may have experienced both serious and non-serious event. Safety analysis set analyzed for AE. Total 153 deaths: 152 adjudicated and 1 occurred after subject discontinued from study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Tofacitinib 5 mg BID

Reporting group description:

Subjects received tofacitinib 5 milligram (mg) oral tablet twice daily (BID) up to 72 months. Subjects were followed up for at least 28 days after last dose of study drug.

Reporting group title	Tofacitinib 10 mg BID

Reporting group description:

Subjects received tofacitinib 10 mg oral tablets (each tablet of 5 mg*2) BID up to 72 months. Dose was reduced to tofacitinib 5 mg BID on or after 19 February 2019 as per Study Protocol Amendment 8. Subjects were followed up for at least 28 days after last dose of study drug.

Reporting group title	TNFi

Reporting group description:

In the US, Puerto Rico and Canada, subjects randomised to TNFi arm received adalimumab 40 mg every other week (QOW) by SC injection and in all other countries, subjects randomised to TNFi arm received etanercept 50 mg once weekly by SC injection up to 72 months. Subjects were followed up for at least 28 days after last dose of study drug.

Serious adverse events	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi
Total subjects affected by serious adverse events			
subjects affected / exposed	373 / 1455 (25.64%)	420 / 1456 (28.85%)	339 / 1451 (23.36%)
number of deaths (all causes)	49	66	38
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Abdominal neoplasm			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Adenoma benign			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Anogenital warts			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
B-cell lymphoma			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder neoplasm			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Breast cancer			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Cholesteatoma			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (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
Colon neoplasm			

subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diffuse large B-cell lymphoma			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Extranodal marginal zone B-cell lymphoma (MALT type)			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Gallbladder neoplasm			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Gastrointestinal lymphoma			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Heavy chain disease			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Lipoma			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Lung neoplasm			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Lung neoplasm malignant			

subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Lymphoma			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoproliferative disorder			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 / 1455 (0.07%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm of pleura			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Meningioma			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Meningioma benign			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Metastatic neoplasm			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Neoplasm			

subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Neuroendocrine carcinoma of the skin			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Non-Hodgkin's lymphoma			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian adenoma			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 granulosa cell tumour			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian neoplasm			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Plasma cell myeloma			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Prostate cancer			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Rectal adenoma			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Rectal cancer			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Rectosigmoid cancer			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cancer			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Schwannoma			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 cancer			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Squamous cell carcinoma			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sweat gland tumour			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid cancer			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Uterine leiomyoma			
subjects affected / exposed	2 / 1455 (0.14%)	2 / 1456 (0.14%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Waldenstrom's macroglobulinaemia			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Vascular disorders			
Aortic intramural haematoma			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Aortic occlusion			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Aortic stenosis			
subjects affected / exposed	2 / 1455 (0.14%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortitis			

subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Circulatory collapse			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Deep vein thrombosis			
subjects affected / exposed	2 / 1455 (0.14%)	7 / 1456 (0.48%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	1 / 3	2 / 7	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extremity necrosis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral artery embolism			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Haematoma			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	2 / 1455 (0.14%)	2 / 1456 (0.14%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive emergency			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive urgency			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Iliac artery occlusion			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Labile blood pressure			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery occlusion			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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	3 / 1455 (0.21%)	0 / 1456 (0.00%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral vascular disorder			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 6	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phlebitis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Shock			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock haemorrhagic			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Superior vena cava syndrome			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (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
Thrombophlebitis superficial			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Thrombosis			

subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicose ulceration			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Varicose vein			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Vasculitis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Venous thrombosis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Venous thrombosis limb			
subjects affected / exposed	3 / 1455 (0.21%)	0 / 1456 (0.00%)	0 / 1451 (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
General disorders and administration site conditions			
Accidental death			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Adverse drug reaction			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Asthenia			

subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest discomfort			
subjects affected / exposed	3 / 1455 (0.21%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complication associated with device			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Death			
subjects affected / exposed	1 / 1455 (0.07%)	2 / 1456 (0.14%)	4 / 1451 (0.28%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device intolerance			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Drug intolerance			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Inflammation			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Mucosal inflammation			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	4 / 1455 (0.27%)	5 / 1456 (0.34%)	5 / 1451 (0.34%)
occurrences causally related to treatment / all	0 / 4	0 / 6	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 1455 (0.07%)	3 / 1456 (0.21%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 1	2 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Immune system disorders			
Anaphylactic reaction			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Anaphylactic shock			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug hypersensitivity			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical polyp			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystocele			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Dysfunctional uterine bleeding			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial hyperplasia			

subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Endometrial hypertrophy			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Endometrial thickening			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Genital prolapse			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Orchitis noninfective			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	0 / 1455 (0.00%)	2 / 1456 (0.14%)	0 / 1451 (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
Postmenopausal haemorrhage			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine polyp			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Uterovaginal prolapse			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Vaginal prolapse			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 1455 (0.07%)	2 / 1456 (0.14%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	4 / 1455 (0.27%)	4 / 1456 (0.27%)	4 / 1451 (0.28%)
occurrences causally related to treatment / all	1 / 8	1 / 4	1 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspiration			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	2 / 1455 (0.14%)	2 / 1456 (0.14%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 2	0 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthmatic crisis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Bronchiectasis			

subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	6 / 1455 (0.41%)	7 / 1456 (0.48%)	4 / 1451 (0.28%)
occurrences causally related to treatment / all	3 / 9	0 / 1	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Dyspnoea			
subjects affected / exposed	5 / 1455 (0.34%)	5 / 1456 (0.34%)	4 / 1451 (0.28%)
occurrences causally related to treatment / all	1 / 6	1 / 5	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (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
Haemoptysis			
subjects affected / exposed	0 / 1455 (0.00%)	2 / 1456 (0.14%)	0 / 1451 (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
Hypoxia			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			

subjects affected / exposed	2 / 1455 (0.14%)	2 / 1456 (0.14%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	1 / 2	0 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Nasal septum deviation			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Obstructive airways disorder			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organising pneumonia			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pickwickian syndrome			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Pleural effusion			
subjects affected / exposed	2 / 1455 (0.14%)	3 / 1456 (0.21%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 3	0 / 3	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			

subjects affected / exposed	2 / 1455 (0.14%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 1455 (0.07%)	2 / 1456 (0.14%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	5 / 1455 (0.34%)	1 / 1456 (0.07%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	1 / 6	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	10 / 1455 (0.69%)	22 / 1456 (1.51%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	3 / 11	3 / 25	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 1455 (0.00%)	2 / 1456 (0.14%)	0 / 1451 (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
Pulmonary thrombosis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory acidosis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory depression			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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 failure			

subjects affected / exposed	7 / 1455 (0.48%)	5 / 1456 (0.34%)	5 / 1451 (0.34%)
occurrences causally related to treatment / all	1 / 7	0 / 5	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid lung			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Status asthmaticus			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Confusional state			
subjects affected / exposed	1 / 1455 (0.07%)	2 / 1456 (0.14%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Depression			
subjects affected / exposed	0 / 1455 (0.00%)	2 / 1456 (0.14%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Major depression			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 1455 (0.00%)	3 / 1456 (0.21%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Suicidal ideation			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Suicide attempt			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	2 / 1455 (0.14%)	2 / 1456 (0.14%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device failure			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Device loosening			
subjects affected / exposed	0 / 1455 (0.00%)	3 / 1456 (0.21%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device occlusion			

subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biopsy endometrium normal			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 alkaline phosphatase increased			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Blood sodium decreased			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Hepatic enzyme increased			
subjects affected / exposed	0 / 1455 (0.00%)	2 / 1456 (0.14%)	0 / 1451 (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
International normalised ratio			

increased			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Lymphocyte count decreased			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Weight decreased			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Acetabulum fracture			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 poisoning			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	2 / 1455 (0.14%)	5 / 1456 (0.34%)	4 / 1451 (0.28%)
occurrences causally related to treatment / all	0 / 2	0 / 5	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Back injury			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Central cord syndrome			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complicated fracture			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Concussion			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Contusion			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Extradural haematoma			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Fall			
subjects affected / exposed	1 / 1455 (0.07%)	2 / 1456 (0.14%)	5 / 1451 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			

subjects affected / exposed	4 / 1455 (0.27%)	3 / 1456 (0.21%)	4 / 1451 (0.28%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	10 / 1455 (0.69%)	5 / 1456 (0.34%)	11 / 1451 (0.76%)
occurrences causally related to treatment / all	0 / 11	0 / 5	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Forearm fracture			
subjects affected / exposed	3 / 1455 (0.21%)	1 / 1456 (0.07%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Graft complication			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Head injury			

subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	5 / 1455 (0.34%)	4 / 1456 (0.27%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	0 / 5	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	5 / 1455 (0.34%)	3 / 1456 (0.21%)	4 / 1451 (0.28%)
occurrences causally related to treatment / all	0 / 5	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 dislocation			
subjects affected / exposed	3 / 1455 (0.21%)	1 / 1456 (0.07%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb injury			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (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
Limb traumatic amputation			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			

subjects affected / exposed	3 / 1455 (0.21%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Meniscus injury			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Multiple fractures			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle rupture			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patella fracture			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Pelvic fracture			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Periprosthetic fracture			
subjects affected / exposed	0 / 1455 (0.00%)	3 / 1456 (0.21%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post laminectomy syndrome			

subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 procedural haemorrhage			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound complication			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Procedural pneumothorax			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Pulmonary contusion			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	3 / 1455 (0.21%)	1 / 1456 (0.07%)	4 / 1451 (0.28%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory fume inhalation disorder			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Rib fracture			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	4 / 1451 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	3 / 1455 (0.21%)	0 / 1456 (0.00%)	0 / 1451 (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
Skin wound			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Spinal compression fracture			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	4 / 1451 (0.28%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haematoma			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Tibia fracture			
subjects affected / exposed	1 / 1455 (0.07%)	3 / 1456 (0.21%)	4 / 1451 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transplant dysfunction			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
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	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Upper limb fracture			
subjects affected / exposed	2 / 1455 (0.14%)	2 / 1456 (0.14%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound necrosis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Wrist fracture			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (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
Congenital, familial and genetic disorders			
Corneal dystrophy			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Developmental hip dysplasia			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Exomphalos			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocele			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
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 left ventricular failure			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (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
Angina pectoris			
subjects affected / exposed	4 / 1455 (0.27%)	2 / 1456 (0.14%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	1 / 4	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	3 / 1455 (0.21%)	3 / 1456 (0.21%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	0 / 3	0 / 3	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve disease			

subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Arrhythmia			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Arrhythmia supraventricular			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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	7 / 1455 (0.48%)	8 / 1456 (0.55%)	6 / 1451 (0.41%)
occurrences causally related to treatment / all	1 / 7	1 / 8	1 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	2 / 1455 (0.14%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 arrest			
subjects affected / exposed	0 / 1455 (0.00%)	4 / 1456 (0.27%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	2 / 1455 (0.14%)	3 / 1456 (0.21%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	2 / 6	0 / 3	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			

subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Cardiac failure chronic			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
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 congestive			
subjects affected / exposed	1 / 1455 (0.07%)	6 / 1456 (0.41%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac pseudoaneurysm			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Cardio-respiratory arrest			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Cardiomyopathy			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Cardiovascular insufficiency			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Chronic left ventricular failure			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congestive cardiomyopathy			

subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Coronary artery disease			
subjects affected / exposed	8 / 1455 (0.55%)	3 / 1456 (0.21%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	2 / 8	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery insufficiency			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery occlusion			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diastolic dysfunction			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cardiomyopathy			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Mitral valve disease			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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	0 / 1455 (0.00%)	1 / 1456 (0.07%)	4 / 1451 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	4 / 1455 (0.27%)	3 / 1456 (0.21%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right ventricular dysfunction			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Sinus node dysfunction			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 1455 (0.00%)	3 / 1456 (0.21%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Ventricular tachycardia			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Nervous system disorders			
Amyotrophic lateral sclerosis			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Basilar artery stenosis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery occlusion			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery stenosis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 1455 (0.00%)	2 / 1456 (0.14%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular disorder			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical cord compression			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical radiculopathy			

subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coma hepatic			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Dementia			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dementia Alzheimer's type			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic neuropathy			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Dizziness			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	0 / 1	1 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Epilepsy			
subjects affected / exposed	0 / 1455 (0.00%)	2 / 1456 (0.14%)	0 / 1451 (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 paralysis			

subjects affected / exposed	0 / 1455 (0.00%)	3 / 1456 (0.21%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Guillain-Barre syndrome			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Headache			
subjects affected / exposed	2 / 1455 (0.14%)	4 / 1456 (0.27%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic encephalopathy			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoaesthesia			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 seizure			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Intercostal neuralgia			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Intracranial aneurysm			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial mass			

subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Ischaemic stroke			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Loss of consciousness			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar radiculopathy			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Lumbosacral radiculopathy			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Metabolic encephalopathy			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Migraine			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Morton's neuralgia			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Myelopathy			

subjects affected / exposed	2 / 1455 (0.14%)	1 / 1456 (0.07%)	0 / 1451 (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
Neuralgia			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral sensorimotor neuropathy			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 herpetic neuralgia			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Postictal paralysis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Presyncope			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Progressive supranuclear palsy			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Quadriplegia			

subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculopathy			
subjects affected / exposed	3 / 1455 (0.21%)	1 / 1456 (0.07%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Restless legs syndrome			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Reversible ischaemic neurological deficit			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ruptured cerebral aneurysm			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	2 / 1455 (0.14%)	1 / 1456 (0.07%)	0 / 1451 (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
Seizure			
subjects affected / exposed	2 / 1455 (0.14%)	3 / 1456 (0.21%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Senile dementia			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Spinal claudication			

subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Spondylitic myelopathy			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 1455 (0.00%)	3 / 1456 (0.21%)	5 / 1451 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thecal sac compression			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Toxic encephalopathy			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	2 / 1455 (0.14%)	8 / 1456 (0.55%)	4 / 1451 (0.28%)
occurrences causally related to treatment / all	0 / 3	2 / 10	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular encephalopathy			

subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	9 / 1455 (0.62%)	4 / 1456 (0.27%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 11	2 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood loss anaemia			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytopenia			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolytic anaemia			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (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
Iron deficiency anaemia			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			

subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Leukopenia			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Lymphadenopathy			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Pancytopenia			
subjects affected / exposed	2 / 1455 (0.14%)	1 / 1456 (0.07%)	4 / 1451 (0.28%)
occurrences causally related to treatment / all	2 / 2	1 / 1	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Acute vestibular syndrome			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Meniere's disease			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Vertigo			
subjects affected / exposed	1 / 1455 (0.07%)	2 / 1456 (0.14%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular disorder			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Eye disorders			
Cataract			
subjects affected / exposed	3 / 1455 (0.21%)	6 / 1456 (0.41%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	0 / 3	0 / 7	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic retinopathy			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Episcleritis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Keratoconus			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Macular hole			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Necrotising retinitis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Retinal detachment			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Retinal vasculitis			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Ulcerative keratitis			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uveitis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal compartment syndrome			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 discomfort			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal distension			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 hernia			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (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
Abdominal incarcerated hernia			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			

subjects affected / exposed	5 / 1455 (0.34%)	1 / 1456 (0.07%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 6	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic gastritis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	4 / 1455 (0.27%)	0 / 1456 (0.00%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	4 / 1455 (0.27%)	2 / 1456 (0.14%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 4	2 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular perforation			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal stenosis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Dysphagia			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (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
Enterocolitis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecaloma			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric polyps			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Gastric ulcer			

subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	3 / 1455 (0.21%)	1 / 1456 (0.07%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 3	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis erosive			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (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
Gastritis haemorrhagic			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 erosion			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	4 / 1451 (0.28%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Gastrooesophageal reflux disease			

subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Hiatus hernia			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Impaired gastric emptying			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Inguinal hernia			
subjects affected / exposed	2 / 1455 (0.14%)	3 / 1456 (0.21%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Intestinal obstruction			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Irritable bowel syndrome			

subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic enteritis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jejunal ulcer			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Jejunal ulcer perforation			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal ulcer			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Large intestine perforation			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mallory-Weiss syndrome			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Melaena			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Mesenteric vein thrombosis			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Nausea			
subjects affected / exposed	3 / 1455 (0.21%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstruction gastric			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Obstructive pancreatitis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Obturator hernia			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Oesophageal food impaction			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Pancreatitis acute			

subjects affected / exposed	1 / 1455 (0.07%)	2 / 1456 (0.14%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 1	2 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis chronic			
subjects affected / exposed	0 / 1455 (0.00%)	2 / 1456 (0.14%)	0 / 1451 (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
Pancreatitis haemorrhagic			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Peptic ulcer			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peptic ulcer haemorrhage			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Peptic ulcer perforation			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Rectal haemorrhage			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	3 / 1455 (0.21%)	1 / 1456 (0.07%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal perforation			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Thrombosis mesenteric vessel			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	2 / 1455 (0.14%)	1 / 1456 (0.07%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	2 / 1455 (0.14%)	1 / 1456 (0.07%)	0 / 1451 (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
Biliary colic			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Cholangitis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			

subjects affected / exposed	1 / 1455 (0.07%)	3 / 1456 (0.21%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	1 / 1	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	3 / 1455 (0.21%)	2 / 1456 (0.14%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 3	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis chronic			
subjects affected / exposed	0 / 1455 (0.00%)	2 / 1456 (0.14%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	4 / 1455 (0.27%)	5 / 1456 (0.34%)	4 / 1451 (0.28%)
occurrences causally related to treatment / all	0 / 4	0 / 5	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cirrhosis alcoholic			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Drug-induced liver injury			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder obstruction			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (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
Gallbladder rupture			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic cirrhosis			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatorenal failure			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Hepatotoxicity			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertransaminasaemia			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decubitus ulcer			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash papular			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Urticaria			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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 and urinary disorders			
Acute kidney injury			
subjects affected / exposed	4 / 1455 (0.27%)	6 / 1456 (0.41%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	1 / 4	1 / 6	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder diverticulum			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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	0 / 1455 (0.00%)	2 / 1456 (0.14%)	0 / 1451 (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
Chronic kidney disease			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
End stage renal disease			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Focal segmental glomerulosclerosis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glomerulonephritis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			

subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal atrophy			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 1455 (0.00%)	2 / 1456 (0.14%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cyst			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 failure			
subjects affected / exposed	0 / 1455 (0.00%)	2 / 1456 (0.14%)	0 / 1451 (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
Renal impairment			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal injury			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Stress urinary incontinence			

subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral stenosis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 retention			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal disorder			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Adrenal haematoma			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthyroidism			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Thyroid mass			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	7 / 1455 (0.48%)	2 / 1456 (0.14%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	0 / 7	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	3 / 1455 (0.21%)	2 / 1456 (0.14%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	4 / 1455 (0.27%)	4 / 1456 (0.27%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 4	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone disorder			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Bone hypertrophy			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis			
subjects affected / exposed	0 / 1455 (0.00%)	2 / 1456 (0.14%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical spinal stenosis			
subjects affected / exposed	1 / 1455 (0.07%)	2 / 1456 (0.14%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Costochondritis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Dupuytren's contracture			

subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Exostosis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Fistula			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Foot deformity			
subjects affected / exposed	1 / 1455 (0.07%)	2 / 1456 (0.14%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemarthrosis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip deformity			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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 degeneration			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc disorder			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (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
Intervertebral disc protrusion			

subjects affected / exposed	4 / 1455 (0.27%)	2 / 1456 (0.14%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint contracture			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint destruction			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint instability			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Knee deformity			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kyphosis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	2 / 1455 (0.14%)	1 / 1456 (0.07%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle tightness			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Muscular weakness			

subjects affected / exposed	0 / 1455 (0.00%)	2 / 1456 (0.14%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (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
Musculoskeletal pain			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Myalgia			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Myopathy			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
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	29 / 1455 (1.99%)	23 / 1456 (1.58%)	16 / 1451 (1.10%)
occurrences causally related to treatment / all	0 / 35	0 / 26	0 / 17
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudarthrosis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Rhabdomyolysis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Rheumatoid arthritis			
subjects affected / exposed	11 / 1455 (0.76%)	10 / 1456 (0.69%)	12 / 1451 (0.83%)
occurrences causally related to treatment / all	1 / 16	2 / 13	2 / 15
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal instability			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Spinal osteoarthritis			
subjects affected / exposed	2 / 1455 (0.14%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal stenosis			

subjects affected / exposed	3 / 1455 (0.21%)	4 / 1456 (0.27%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondyloarthropathy			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Spondylolisthesis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial cyst			
subjects affected / exposed	0 / 1455 (0.00%)	2 / 1456 (0.14%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial disorder			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Tendon disorder			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Tendonitis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tenosynovitis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic spinal stenosis			

subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	3 / 1455 (0.21%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	2 / 3	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute pulmonary histoplasmosis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute sinusitis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenovirus infection			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Anal abscess			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Appendiceal abscess			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 / 1455 (0.27%)	4 / 1456 (0.27%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	1 / 4	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Arthritis bacterial			
subjects affected / exposed	2 / 1455 (0.14%)	4 / 1456 (0.27%)	4 / 1451 (0.28%)
occurrences causally related to treatment / all	1 / 3	3 / 4	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
subjects affected / exposed	0 / 1455 (0.00%)	2 / 1456 (0.14%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Bacterial sepsis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Bone tuberculosis			

subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Brain abscess			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Breast abscess			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Bronchiolitis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	10 / 1455 (0.69%)	9 / 1456 (0.62%)	7 / 1451 (0.48%)
occurrences causally related to treatment / all	4 / 10	4 / 10	4 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis bacterial			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Bronchitis viral			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Bursitis infective			

subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
COVID-19 pneumonia			
subjects affected / exposed	1 / 1455 (0.07%)	5 / 1456 (0.34%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 1	2 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carbuncle			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Cellulitis			
subjects affected / exposed	12 / 1455 (0.82%)	13 / 1456 (0.89%)	15 / 1451 (1.03%)
occurrences causally related to treatment / all	5 / 14	10 / 14	5 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis staphylococcal			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis infective			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chorioretinitis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Chronic sinusitis			

subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Clostridium difficile colitis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic abscess			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Complicated appendicitis			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus chorioretinitis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Cytomegalovirus infection			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Dengue fever			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	2 / 1455 (0.14%)	2 / 1456 (0.14%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	2 / 3	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea infectious			

subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Disseminated tuberculosis			
subjects affected / exposed	0 / 1455 (0.00%)	2 / 1456 (0.14%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated varicella zoster virus infection			
subjects affected / exposed	0 / 1455 (0.00%)	4 / 1456 (0.27%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	7 / 1455 (0.48%)	6 / 1456 (0.41%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	2 / 7	4 / 7	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis meningococcal			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epididymitis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Erysipelas			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Escherichia infection			

subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia pyelonephritis			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	0 / 1451 (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
Escherichia sepsis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Escherichia urinary tract infection			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
External ear cellulitis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Extradural abscess			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye infection			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Gangrene			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			

subjects affected / exposed	4 / 1455 (0.27%)	7 / 1456 (0.48%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	3 / 4	3 / 7	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis bacterial			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 viral			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
H1N1 influenza			
subjects affected / exposed	0 / 1455 (0.00%)	2 / 1456 (0.14%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes oesophagitis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes ophthalmic			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Herpes virus infection			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Herpes zoster			

subjects affected / exposed	9 / 1455 (0.62%)	11 / 1456 (0.76%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	7 / 9	11 / 11	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Histoplasmosis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Infected bite			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Infectious pleural effusion			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	4 / 1455 (0.27%)	3 / 1456 (0.21%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	3 / 4	1 / 3	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral discitis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint abscess			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver abscess			

subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Lower respiratory tract infection			
subjects affected / exposed	2 / 1455 (0.14%)	3 / 1456 (0.21%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	2 / 2	2 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung abscess			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Lyme disease			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Medical device site joint infection			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis bacterial			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningoencephalitis herpetic			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Muscle abscess			

subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nail infection			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Neuroborreliosis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurocryptococcosis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Ophthalmic herpes zoster			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Orchitis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Osteomyelitis			
subjects affected / exposed	2 / 1455 (0.14%)	3 / 1456 (0.21%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	2 / 2	1 / 3	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis acute			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Parainfluenzae virus infection			

subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Parotid abscess			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parotitis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Pelvic abscess			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic inflammatory disease			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Pericarditis tuberculous			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Perihepatic abscess			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Peritoneal tuberculosis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	50 / 1455 (3.44%)	56 / 1456 (3.85%)	43 / 1451 (2.96%)
occurrences causally related to treatment / all	33 / 60	41 / 63	26 / 46
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	2 / 1455 (0.14%)	1 / 1456 (0.07%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	2 / 2	0 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia fungal			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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 influenzal			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia legionella			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia mycoplasmal			

subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Pneumonia pneumococcal			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 staphylococcal			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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 procedural infection			
subjects affected / exposed	2 / 1455 (0.14%)	1 / 1456 (0.07%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural pneumonia			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural sepsis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Postoperative wound infection			
subjects affected / exposed	3 / 1455 (0.21%)	2 / 1456 (0.14%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulpitis dental			

subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	2 / 1455 (0.14%)	2 / 1456 (0.14%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	2 / 2	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	2 / 1455 (0.14%)	1 / 1456 (0.07%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyometra			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Rectal abscess			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal abscess			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal tuberculosis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 1455 (0.07%)	2 / 1456 (0.14%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	1 / 1	2 / 3	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection viral			

subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal abscess			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonella sepsis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Sepsis			
subjects affected / exposed	6 / 1455 (0.41%)	6 / 1456 (0.41%)	5 / 1451 (0.34%)
occurrences causally related to treatment / all	5 / 6	3 / 6	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	4 / 1455 (0.27%)	9 / 1456 (0.62%)	3 / 1451 (0.21%)
occurrences causally related to treatment / all	1 / 4	3 / 9	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinobronchitis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis fungal			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Soft tissue infection			
subjects affected / exposed	1 / 1455 (0.07%)	2 / 1456 (0.14%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			

subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic candida			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Tick-borne fever			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth abscess			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Tracheobronchitis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Tubo-ovarian abscess			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Upper respiratory tract infection			
subjects affected / exposed	4 / 1455 (0.27%)	2 / 1456 (0.14%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	3 / 4	1 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	14 / 1455 (0.96%)	14 / 1456 (0.96%)	9 / 1451 (0.62%)
occurrences causally related to treatment / all	10 / 16	9 / 14	5 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 1455 (0.00%)	3 / 1456 (0.21%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	0 / 0	2 / 3	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 1455 (0.07%)	2 / 1456 (0.14%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	2 / 1451 (0.14%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection staphylococcal			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	0 / 1451 (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
Dehydration			
subjects affected / exposed	1 / 1455 (0.07%)	1 / 1456 (0.07%)	4 / 1451 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			

subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus inadequate control			
subjects affected / exposed	2 / 1455 (0.14%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrolyte imbalance			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Fluid overload			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Hypercalcaemia			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemic hyperosmolar nonketotic syndrome			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			

subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Hypernatraemia			
subjects affected / exposed	0 / 1455 (0.00%)	1 / 1456 (0.07%)	0 / 1451 (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
Hypertriglyceridaemia			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypochloraemia			
subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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
Hypoglycaemia			
subjects affected / exposed	0 / 1455 (0.00%)	2 / 1456 (0.14%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 1455 (0.07%)	2 / 1456 (0.14%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	2 / 1455 (0.14%)	4 / 1456 (0.27%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ketoacidosis			
subjects affected / exposed	0 / 1455 (0.00%)	0 / 1456 (0.00%)	1 / 1451 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitamin D deficiency			

subjects affected / exposed	1 / 1455 (0.07%)	0 / 1456 (0.00%)	0 / 1451 (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

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

Non-serious adverse events	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	TNFi
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1108 / 1455 (76.15%)	1127 / 1456 (77.40%)	1056 / 1451 (72.78%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	67 / 1455 (4.60%)	75 / 1456 (5.15%)	48 / 1451 (3.31%)
occurrences (all)	85	100	65
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	177 / 1455 (12.16%)	160 / 1456 (10.99%)	159 / 1451 (10.96%)
occurrences (all)	218	197	202
Vascular disorders			
Hypertension			
subjects affected / exposed	129 / 1455 (8.87%)	152 / 1456 (10.44%)	127 / 1451 (8.75%)
occurrences (all)	143	175	142
Nervous system disorders			
Headache			
subjects affected / exposed	50 / 1455 (3.44%)	75 / 1456 (5.15%)	64 / 1451 (4.41%)
occurrences (all)	56	91	79
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	75 / 1455 (5.15%)	100 / 1456 (6.87%)	73 / 1451 (5.03%)
occurrences (all)	90	131	81
Lymphopenia			
subjects affected / exposed	107 / 1455 (7.35%)	151 / 1456 (10.37%)	36 / 1451 (2.48%)
occurrences (all)	186	291	57
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	99 / 1455 (6.80%)	81 / 1456 (5.56%)	74 / 1451 (5.10%)
occurrences (all)	114	98	90
Nausea			
subjects affected / exposed	67 / 1455 (4.60%)	96 / 1456 (6.59%)	61 / 1451 (4.20%)
occurrences (all)	82	112	69
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	77 / 1455 (5.29%)	70 / 1456 (4.81%)	72 / 1451 (4.96%)
occurrences (all)	86	89	87
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	111 / 1455 (7.63%)	90 / 1456 (6.18%)	124 / 1451 (8.55%)
occurrences (all)	150	128	173
Back pain			
subjects affected / exposed	101 / 1455 (6.94%)	113 / 1456 (7.76%)	112 / 1451 (7.72%)
occurrences (all)	120	132	124
Osteoarthritis			
subjects affected / exposed	84 / 1455 (5.77%)	71 / 1456 (4.88%)	77 / 1451 (5.31%)
occurrences (all)	102	79	91
Rheumatoid arthritis			
subjects affected / exposed	183 / 1455 (12.58%)	188 / 1456 (12.91%)	202 / 1451 (13.92%)
occurrences (all)	276	273	290
Infections and infestations			
Bronchitis			
subjects affected / exposed	221 / 1455 (15.19%)	243 / 1456 (16.69%)	168 / 1451 (11.58%)
occurrences (all)	334	313	215
Gastroenteritis			
subjects affected / exposed	61 / 1455 (4.19%)	76 / 1456 (5.22%)	52 / 1451 (3.58%)
occurrences (all)	78	89	56
Herpes zoster			
subjects affected / exposed	175 / 1455 (12.03%)	160 / 1456 (10.99%)	59 / 1451 (4.07%)
occurrences (all)	188	175	59
Influenza			
subjects affected / exposed	92 / 1455 (6.32%)	95 / 1456 (6.52%)	71 / 1451 (4.89%)
occurrences (all)	120	117	104

Latent tuberculosis			
subjects affected / exposed	89 / 1455 (6.12%)	72 / 1456 (4.95%)	94 / 1451 (6.48%)
occurrences (all)	89	73	94
Nasopharyngitis			
subjects affected / exposed	168 / 1455 (11.55%)	172 / 1456 (11.81%)	164 / 1451 (11.30%)
occurrences (all)	231	248	233
Pharyngitis			
subjects affected / exposed	87 / 1455 (5.98%)	81 / 1456 (5.56%)	75 / 1451 (5.17%)
occurrences (all)	103	107	96
Sinusitis			
subjects affected / exposed	97 / 1455 (6.67%)	81 / 1456 (5.56%)	94 / 1451 (6.48%)
occurrences (all)	134	132	133
Upper respiratory tract infection			
subjects affected / exposed	319 / 1455 (21.92%)	318 / 1456 (21.84%)	264 / 1451 (18.19%)
occurrences (all)	564	533	415
Urinary tract infection			
subjects affected / exposed	190 / 1455 (13.06%)	220 / 1456 (15.11%)	186 / 1451 (12.82%)
occurrences (all)	308	372	284

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 July 2013	To reduce the study from 8 years to 5 years, to increased N from 3900 to approximately 4000, to eliminate the double-blind substudy, to change the comparator from all adalimumab to adalimumab in US, Puerto Rico and Canada with etanercept in the rest of world, to reduce joint counts from 66/68 to 28 at every visit, to remove the following Patient Reported Outcomes (PROs): Medical Outcomes Study (MOS) Sleep Scale, Functional Assessment of Chronic Illness Therapy-fatigue (FACIT-fatigue), and Rheumatoid Arthritis (RA) Healthcare Resource Utilization Questionnaires and reduced the frequency of 36-Item Short Form Health Survey (SF-36), EuroQol EQ-5D Health State Profile (EuroQol EQ-5D), and Work Productivity and Activity Impairment Questionnaires, eliminated routine electrocardiograms, except at screening Visit and end of study Visit, to remove laboratory testing not used in safety evaluation of either tofacitinib or TNFi's, to align monitoring and discontinuation criteria with the US approved labeling.
20 November 2013	To make typographical corrections and clarifications, to make changes to reporting processes for the primary safety endpoints to limit their inclusion in AE tables reviewed outside the blinded Steering Committee, to add a washout period for rituximab as a prohibited concomitant disease-modifying anti-rheumatic drug (DMARD).
18 March 2019	To reduce treatment in the tofacitinib 10 mg BID arm to 5 mg BID in response to a recommendation from the Data Safety Monitoring Board for a safety signal, to add requirement for all subjects to provide a consent addendum, which they were required to sign agreeing to continue in the study, deep vein thrombosis, pulmonary emboli, arterial thrombosis and arterial emboli were added to the cardiovascular adjudication charter and were noted as additional events to be adjudicated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported