Clinical trial results:
A Randomized, Double-blind, Placebo- and Active-controlled, Multicenter, Phase 3 Study to Assess the Efficacy and Safety of Filgotinib Administered for 52 weeks in Combination with Methotrexate to Subjects with Moderately to Severely Active Rheumatoid Arthritis Who Have an Inadequate Response to Methotrexate

Summary

EudraCT number	2016-000568-41
Trial protocol	SK GB BE HU CZ DE ES BG PL NL IT
Global end of trial date	20 June 2019

Results information

Result version number	v1
This version publication date	05 July 2020
First version publication date	05 July 2020

Trial information

Trial identification

Sponsor protocol code	GS-US-417-0301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02889796
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.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	20 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 July 2018
Global end of trial reached?	Yes
Global end of trial date	20 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the effects of filgotinib versus placebo for the treatment of signs and symptoms of rheumatoid arthritis (RA) as measured by the percentage of participants achieving an American College of Rheumatology 20% improvement response (ACR20) at week 12.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy:

Methotrexate (MTX) was used across all the arms as background therapy.

Evidence for comparator: -

Actual start date of recruitment	30 August 2016
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	Poland: 299
Country: Number of subjects enrolled	Ukraine: 235
Country: Number of subjects enrolled	United States: 200
Country: Number of subjects enrolled	Japan: 147
Country: Number of subjects enrolled	India: 137
Country: Number of subjects enrolled	Mexico: 125
Country: Number of subjects enrolled	Russian Federation: 118
Country: Number of subjects enrolled	Argentina: 57
Country: Number of subjects enrolled	Hungary: 47
Country: Number of subjects enrolled	Taiwan: 44
Country: Number of subjects enrolled	Bulgaria: 34
Country: Number of subjects enrolled	Czech Republic: 34
Country: Number of subjects enrolled	South Africa: 34

Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 33
Country: Number of subjects enrolled	Romania: 31
Country: Number of subjects enrolled	Spain: 30
Country: Number of subjects enrolled	Thailand: 23
Country: Number of subjects enrolled	Serbia: 21
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	New Zealand: 18
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	Canada: 12
Country: Number of subjects enrolled	Israel: 11
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	Slovakia: 8
Country: Number of subjects enrolled	Hong Kong: 7
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Ireland: 1
Worldwide total number of subjects	1759
EEA total number of subjects	536

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)	1425
From 65 to 84 years	333
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Asia, South Africa, Australia, Europe, North America, South America and New Zealand. The first participant was screened on 30 August 2016. The last study visit occurred on 20 June 2019.

Pre-assignment

Screening details:

2582 participants were screened. Completed in the Placebo never received filgotinib arm includes participants who completed 24 weeks of placebo treatment and were not rerandomized to Filgotinib 200 mg or 100 mg groups.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Filgotinib 200 mg

Arm description:

Participants were administered a filgotinib 200 mg tablet orally, once daily + placebo (PBO) to match [PTM] filgotinib 100 mg tablet orally, once daily + PTM adalimumab 40 mg subcutaneous (SC) injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 52.1 weeks.

Arm type	Experimental
Investigational medicinal product name	Filgotinib
Investigational medicinal product code	
Other name	GS-6034, GLPG0634
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg administered once daily

Investigational medicinal product name	PTM Filgotinib 100 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

PTM filgotinib 100 mg administered once daily

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

Dosage and administration details:

PTM adalimumab 40 mg administered once every 2 weeks

Arm title	Filgotinib 100 mg

Arm description:

Participants were administered a filgotinib 100 mg tablet orally, once daily + PTM filgotinib 200 mg

tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 52.1 weeks.

Arm type	Experimental
Investigational medicinal product name	Filgotinib
Investigational medicinal product code	
Other name	GS-6034, GLPG0634
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg administered once daily

Investigational medicinal product name	PTM Filgotinib 200 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

PTM filgotinib 200 mg administered once daily

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

Dosage and administration details:

PTM adalimumab 40 mg administered once every 2 weeks

Arm title	Adalimumab

Arm description:

Participants were administered PTM filgotinib 200 mg tablet orally, once daily + PTM filgotinib 100 mg tablet orally, once daily + adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 52.1 weeks.

Arm type	Active comparator
Investigational medicinal product name	PTM Filgotinib 200 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

PTM filgotinib 200 mg administered once daily

Investigational medicinal product name	PTM Filgotinib 100 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

PTM filgotinib 100 mg administered once daily

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

Dosage and administration details:

40 mg administered once every 2 weeks

Arm title	Placebo to Filgotinib 200 mg

Arm description:

Participants in the placebo arm were administered a PTM filgotinib 200 mg tablet orally, once daily+ a PTM filgotinib 100 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 24 weeks. Then the participants in the placebo arm were rerandomized to filgotinib 200 mg and were administered a filgotinib 200 mg tablet orally, once daily + PTM filgotinib 100 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 28.1 weeks.

Arm type	Experimental
Investigational medicinal product name	PTM Filgotinib 200 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

PTM filgotinib 200 mg administered once daily

Investigational medicinal product name	PTM Filgotinib 100 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

PTM filgotinib 100 mg administered once daily

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

Dosage and administration details:

PTM adalimumab 40 mg administered once every 2 weeks

Investigational medicinal product name	Filgotinib
Investigational medicinal product code	
Other name	GS-6034, GLPG0634
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg administered once daily

Arm title	Placebo to Filgotinib 100 mg

Arm description:

Participants in the placebo arm were administered a PTM filgotinib 200 mg tablet orally, once daily+ a PTM filgotinib 100 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 24 weeks. Then the participants in the placebo arm were rerandomized to filgotinib 100 mg and were administered a filgotinib 100 mg tablet orally, once daily + PTM filgotinib 200 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 28.1 weeks.

Arm type	Experimental
Investigational medicinal product name	PTM Filgotinib 200 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

PTM filgotinib 200 mg administered once daily

Investigational medicinal product name	PTM Filgotinib 100 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

PTM filgotinib 100 mg administered once daily

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

Dosage and administration details:

PTM adalimumab 40 mg administered once every 2 weeks

Investigational medicinal product name	Filgotinib
Investigational medicinal product code	
Other name	GS-6034, GLPG0634
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg administered once daily

Arm title	Placebo never received Filgotinib

Arm description:

Participants in the placebo arm were administered a PTM filgotinib 200 mg tablet orally, once daily+ a PTM filgotinib 100 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 24 weeks.

Arm type	Placebo
Investigational medicinal product name	PTM Filgotinib 200 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

PTM filgotinib 200 mg administered once daily

Investigational medicinal product name	PTM Filgotinib 100 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

PTM filgotinib 100 mg administered once daily

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

Dosage and administration details:

PTM adalimumab 40 mg administered once every 2 weeks

Number of subjects in period 1[1]	Filgotinib 200 mg	Filgotinib 100 mg	Adalimumab
Started	475	480	325
Completed	424	422	281
Not completed	51	58	44
Protocol violation	-	1	3
Death	1	1	-
Pregnancy	-	1	1
Adverse event	17	8	8
Non-compliance with study drug	-	2	-
Investigator`s discretion	10	9	10
Withdrew consent	18	29	20
Lost to follow-up	5	7	2

Number of subjects in period 1[1]	Placebo to Filgotinib 200 mg	Placebo to Filgotinib 100 mg	Placebo never received Filgotinib
Started	190	191	94
Completed	181	185	24
Not completed	9	6	70
Protocol violation	-	-	4
Death	1	-	1
Pregnancy	-	-	-
Adverse event	4	1	7
Non-compliance with study drug	-	1	2
Investigator`s discretion	3	-	15
Withdrew consent	1	2	35
Lost to follow-up	-	2	6

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Four participants who were randomized but did not receive the study drug are not included in the subject disposition table.

Baseline characteristics

Reporting groups

Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	1755	1755	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	53.0		
standard deviation	± 12.7	-	
Gender categorical Units: Subjects			
Female	1435	1435	
Male	320	320	
Race			
For participants in Not Permitted category: local regulators did not allow collection of race information.			
Units: Subjects			
American Indian or Alaska Native	103	103	
Asian: Japanese	147	147	
Asian: Chinese/Taiwanese/Hong Kong Chinese	51	51	
Asian: Korean	34	34	
Asian: Other	179	179	
Black or African American	35	35	
Native Hawaiian or Pacific Islander	3	3	
White	1184	1184	
Other	17	17	
Not Permitted	2	2	
Ethnicity			
For participants in Not Permitted category: local regulators did not allow collection of ethnicity information.			
Units: Subjects			
Hispanic or Latino	262	262	
Not Hispanic or Latino	1471	1471	
Not Permitted	22	22	

Subject analysis sets

Subject analysis set title	Filgotinib 200 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were administered a filgotinib 200 mg tablet orally, once daily + a placebo to match (PTM) filgotinib 100 mg tablet orally, once daily + PTM adalimumab 40 mg subcutaneous (SC) injection, once every 2 weeks in addition to a weekly stable dose of methotrexate (MTX), orally for median exposure of 52.1 weeks.

Subject analysis set title	Filgotinib 100 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were administered a filgotinib 100 mg tablet orally, once daily + a PTM filgotinib 200 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 52.1 weeks.

Subject analysis set title	Adalimumab
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were administered a PTM filgotinib 200 mg tablet orally, once daily + a PTM filgotinib 100 mg tablet orally, once daily + adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 52.1 weeks.

Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

The Placebo arm included all participants who received placebo in the study. Participants were administered a PTM filgotinib 200 mg tablet orally, once daily+ a PTM filgotinib 100 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 24 weeks. Participants could be rerandomized to filgotinib 200 mg or 100 mg groups.

Reporting group values	Filgotinib 200 mg	Filgotinib 100 mg	Adalimumab
Number of subjects	475	480	325
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	52.0	53.0	53.0
standard deviation	± 12.8	± 12.6	± 12.9
Gender categorical Units: Subjects			
Female	379	399	266
Male	96	81	59
Race			
For participants in Not Permitted category: local regulators did not allow collection of race information.			
Units: Subjects			
American Indian or Alaska Native	27	27	20
Asian: Japanese	40	41	28
Asian: Chinese/Taiwanese/Hong Kong Chinese	13	12	8
Asian: Korean	13	10	4
Asian: Other	56	52	25
Black or African American	6	7	10
Native Hawaiian or Pacific Islander	1	0	0
White	312	324	229
Other	7	6	1
Not Permitted	0	1	0
Ethnicity			
For participants in Not Permitted category: local regulators did not allow collection of ethnicity information.			
Units: Subjects			
Hispanic or Latino	67	71	54
Not Hispanic or Latino	404	399	268

Not Permitted	4	10	3

Reporting group values	Placebo		
Number of subjects	475		
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	53.0		
standard deviation	± 12.8		
Gender categorical Units: Subjects			
Female	391		
Male	84		
Race			
For participants in Not Permitted category: local regulators did not allow collection of race information.			
Units: Subjects			
American Indian or Alaska Native	29		
Asian: Japanese	38		
Asian: Chinese/Taiwanese/Hong Kong Chinese	18		
Asian: Korean	7		
Asian: Other	46		
Black or African American	12		
Native Hawaiian or Pacific Islander	2		
White	319		
Other	3		
Not Permitted	1		
Ethnicity			
For participants in Not Permitted category: local regulators did not allow collection of ethnicity information.			
Units: Subjects			
Hispanic or Latino	70		
Not Hispanic or Latino	400		
Not Permitted	5		

End points reporting groups

Reporting group title	Filgotinib 200 mg

Reporting group description:

Participants were administered a filgotinib 200 mg tablet orally, once daily + placebo (PBO) to match [PTM] filgotinib 100 mg tablet orally, once daily + PTM adalimumab 40 mg subcutaneous (SC) injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 52.1 weeks.

Reporting group title	Filgotinib 100 mg

Reporting group description:

Participants were administered a filgotinib 100 mg tablet orally, once daily + PTM filgotinib 200 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 52.1 weeks.

Reporting group title	Adalimumab

Reporting group description:

Participants were administered PTM filgotinib 200 mg tablet orally, once daily + PTM filgotinib 100 mg tablet orally, once daily + adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 52.1 weeks.

Reporting group title	Placebo to Filgotinib 200 mg

Reporting group description:

Participants in the placebo arm were administered a PTM filgotinib 200 mg tablet orally, once daily+ a PTM filgotinib 100 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 24 weeks. Then the participants in the placebo arm were rerandomized to filgotinib 200 mg and were administered a filgotinib 200 mg tablet orally, once daily + PTM filgotinib 100 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 28.1 weeks.

Reporting group title	Placebo to Filgotinib 100 mg

Reporting group description:

Participants in the placebo arm were administered a PTM filgotinib 200 mg tablet orally, once daily+ a PTM filgotinib 100 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 24 weeks. Then the participants in the placebo arm were rerandomized to filgotinib 100 mg and were administered a filgotinib 100 mg tablet orally, once daily + PTM filgotinib 200 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 28.1 weeks.

Reporting group title	Placebo never received Filgotinib

Reporting group description:

Participants in the placebo arm were administered a PTM filgotinib 200 mg tablet orally, once daily+ a PTM filgotinib 100 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 24 weeks.

Subject analysis set title	Filgotinib 200 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were administered a filgotinib 200 mg tablet orally, once daily + a placebo to match (PTM) filgotinib 100 mg tablet orally, once daily + PTM adalimumab 40 mg subcutaneous (SC) injection, once every 2 weeks in addition to a weekly stable dose of methotrexate (MTX), orally for median exposure of 52.1 weeks.

Subject analysis set title	Filgotinib 100 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were administered a filgotinib 100 mg tablet orally, once daily + a PTM filgotinib 200 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 52.1 weeks.

Subject analysis set title	Adalimumab
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were administered a PTM filgotinib 200 mg tablet orally, once daily + a PTM filgotinib 100 mg tablet orally, once daily + adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 52.1 weeks.

Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

The Placebo arm included all participants who received placebo in the study. Participants were administered a PTM filgotinib 200 mg tablet orally, once daily+ a PTM filgotinib 100 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 24 weeks. Participants could be rerandomized to filgotinib 200 mg or 100 mg groups.

Primary: Percentage of Participants who Achieved an American College of Rheumatology (ACR) 20% Improvement (ACR20) Response at Week 12

End point title	Percentage of Participants who Achieved an American College of Rheumatology (ACR) 20% Improvement (ACR20) Response at Week 12[1]

End point description:

ACR20 response is achieved when the participant has: ≥20% improvement (reduction) from baseline in tender joint count based on 68 joints (TJC68), swollen joint count based on 66 joints (SJC66) and in at least 3 of the following 5 items: physician's global assessment of disease activity (PGA), subject's global assessment of disease activity (SGA) using visual analog scale (VAS) on a scale of 0 (no disease activity) to 100 (maximum disease activity),participant`s pain assessment using VAS on a scale of 0 (no pain) to 100 (unbearable pain),health assessment questionnaire disability index (HAQ-DI) score contains 20 questions,8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities scored on a scale of 0 (without difficulty) to 3 (unable to do);high-sensitivity C-reactive protein (hsCRP). Full Analysis Set included participants who were randomized and received at least 1 dose of study drug. Participants with missing outcomes were set as non-responders.

End point type	Primary

End point timeframe:

Week 12

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The Baseline period arms for Placebo [Placebo to Filgotinib 200 mg, Placebo to Filgotinib 100 mg, and Placebo never received Filgotinib] were combined to present data for the total number of participants who received Placebo.

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Adalimumab	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	475	480	325	475
Units: percentage of participants				
number (confidence interval 95%)	76.6 (72.7 to 80.5)	69.8 (65.6 to 74.0)	70.5 (65.3 to 75.6)	49.9 (45.3 to 54.5)

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo
Comparison groups	Filgotinib 200 mg v Placebo

Number of subjects included in analysis	950
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [2]
Method	Regression, Logistic
Parameter estimate	Difference in Response Rates
Point estimate	26.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.6
upper limit	32.8

Notes:

[2] - P-value was calculated from the logistic regression with treatment groups and stratification factors in the model.

Statistical analysis title	Filgotinib 100 mg vs Placebo
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	955
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [3]
Method	Regression, Logistic
Parameter estimate	Difference in Response Rates
Point estimate	19.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.6
upper limit	26.2

Notes:

[3] - P-value was calculated from the logistic regression with treatment groups and stratification factors in the model.

Secondary: Percentage of Participants who Achieved Disease Activity Score for 28 Joint Count Using C-Reactive Protein [DAS28 (CRP)] ≤ 3.2 at Week 12

End point title	Percentage of Participants who Achieved Disease Activity Score for 28 Joint Count Using C-Reactive Protein [DAS28 (CRP)] ≤ 3.2 at Week 12[4]

End point description:

The DAS28 score is a measure of the participant's disease activity calculated using the tender joint counts (28 joints), swollen joint counts (28 joints), Patient's Global Assessment of Disease Activity (visual analog scale: 0 = no disease activity to 100 = maximum disease activity), and hsCRP for a total possible score of 1 to 9.4. Higher values indicate higher disease activity. Participants in the Full Analysis Set were analyzed. Participants with missing outcomes were set as non-responders.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The Baseline period arms for Placebo [Placebo to Filgotinib 200 mg, Placebo to Filgotinib 100 mg, and Placebo never received Filgotinib] were combined to present data for the total number of participants who received Placebo.

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Adalimumab	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	475	480	325	475
Units: percentage of participants				
number (confidence interval 95%)	49.7 (45.1 to 54.3)	38.8 (34.3 to 43.2)	43.4 (37.8 to 48.9)	23.4 (19.5 to 27.3)

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo
Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	950
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [5]
Method	Regression, Logistic
Parameter estimate	Difference in Response Rates
Point estimate	26.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.2
upper limit	32.4

Notes:

[5] - P-value was calculated from the logistic regression with treatment groups and stratification factors in the model.

Statistical analysis title	Filgotinib 100 mg vs Placebo
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	955
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [6]
Method	Regression, Logistic
Parameter estimate	Difference in Response Rates
Point estimate	15.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.4
upper limit	21.4

Notes:

[6] - P-value was calculated from the logistic regression with treatment groups and stratification factors in the model.

Statistical analysis title	Filgotinib 200 mg vs Adalimumab
Comparison groups	Filgotinib 200 mg v Adalimumab

Number of subjects included in analysis	800
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001 [7]
Method	Regression, Logistic

Notes:

[7] - P-value of non-inferiority test was calculated from approach proposed by [Liu 2014].

Statistical analysis title	Filgotinib 100 mg vs Adalimumab
Comparison groups	Filgotinib 100 mg v Adalimumab
Number of subjects included in analysis	805
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.054 [8]
Method	Regression, Logistic

Notes:

[8] - P-value of non-inferiority test was calculated from approach proposed by [Liu 2014].

Statistical analysis title	Filgotinib 200 mg vs Adalimumab
Comparison groups	Filgotinib 200 mg v Adalimumab
Number of subjects included in analysis	800
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.069 [9]
Method	Regression, Logistic
Parameter estimate	Difference in Response Rates
Point estimate	6.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	13.6

Notes:

[9] - P-value was calculated from the logistic regression with treatment groups and stratification factors in the model.

Statistical analysis title	Filgotinib 100 mg vs Adalimumab
Comparison groups	Filgotinib 100 mg v Adalimumab
Number of subjects included in analysis	805
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.18 [10]
Method	Regression, Logistic
Parameter estimate	Difference in Response Rates
Point estimate	-4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.8
upper limit	2.6

Notes:

[10] - P-value was calculated from the logistic regression with treatment groups and stratification factors in the model.

Secondary: Change from Baseline in the Health Assessment Questionnaire-Disability Index (HAQ-DI) Score at Week 12

End point title	Change from Baseline in the Health Assessment Questionnaire-Disability Index (HAQ-DI) Score at Week 12[11]

End point description:

The HAQ-DI score is defined as the average of the scores of eight functional categories (dressing and grooming, arising, eating, walking, hygiene, reach, grip, and other activities), usually completed by the participant. Responses in each functional category are collected as 0 (without any difficulty) to 3 (unable to do a task in that area), with or without aids or devices. The eight category scores are averaged into an overall HAQ-DI score on a scale from 0 (no disability) to 3 (completely disabled). When 6 or more categories are non-missing, total possible score is 3. If more than 2 categories are missing, the HAQ-DI score is set to missing. Negative change from baseline indicates improvement (less disability). Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 12

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The Baseline period arms for Placebo [Placebo to Filgotinib 200 mg, Placebo to Filgotinib 100 mg, and Placebo never received Filgotinib] were combined to present data for the total number of participants who received Placebo.

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Adalimumab	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	475	480	325	475
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline	1.59 (± 0.611)	1.55 (± 0.625)	1.59 (± 0.600)	1.63 (± 0.613)
Change at Week 12 (n=457, 459, 311, 435)	-0.69 (± 0.613)	-0.56 (± 0.564)	-0.61 (± 0.560)	-0.42 (± 0.544)

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo
Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	950
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	< 0.001 [13]
Method	Mixed effects model for repeated measure
Parameter estimate	Least Squares Mean Difference
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	-0.22

Variability estimate	Standard error of the mean
Dispersion value	0.034

Notes:

[12] - LS-Mean, 95% CI, and P-value were provided from mixed effects model for repeated measure (MMRM). Missing change scores were not imputed using the MMRM approach assuming an unstructured variance-covariance matrix for the repeated measures.
[13] - MMRM model included treatment, visit, treatment by visit, stratification factors, and baseline value as fixed effects, and subjects being the random effect.

Statistical analysis title	Filgotinib 100 mg vs Placebo
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	955
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	< 0.001 [15]
Method	MMRM
Parameter estimate	Least Squares Mean Difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.034

Notes:

[14] - LS-Mean, 95% CI, and P-value were provided from MMRM. Missing change scores were not imputed using the MMRM approach assuming an unstructured variance-covariance matrix for the repeated measures.
[15] - MMRM model included treatment, visit, treatment by visit, stratification factors, and baseline value as fixed effects, and subjects being the random effect.

Secondary: Percentage of Participants who Achieved DAS28 (CRP) < 2.6 at Week 24

End point title	Percentage of Participants who Achieved DAS28 (CRP) < 2.6 at Week 24[16]

End point description:

The DAS28 score is a measure of the participant's disease activity calculated using the tender joint counts (28 joints), swollen joint counts (28 joints), Patient's Global Assessment of Disease Activity (visual analog scale: 0 = no disease activity to 100 = maximum disease activity), and hsCRP for a total possible score of 1 to 9.4. Higher values indicate higher disease activity. Participants in the Full Analysis Set were analyzed. Participants with missing outcomes were set as non-responders.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The Baseline period arms for Placebo [Placebo to Filgotinib 200 mg, Placebo to Filgotinib 100 mg, and Placebo never received Filgotinib] were combined to present data for the total number of participants who received Placebo.

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Adalimumab	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	475	480	325	475
Units: percentage of participants				
number (confidence interval 95%)	48.4 (43.8 to 53.0)	35.2 (30.8 to 39.6)	35.7 (30.3 to 41.1)	16.2 (12.8 to 19.6)

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo
Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	950
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [17]
Method	Regression, Logistic
Parameter estimate	Difference in Response Rates
Point estimate	32.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	26.4
upper limit	38

Notes:

[17] - P-value was calculated from the logistic regression with treatment groups and stratification factors in the model.

Statistical analysis title	Filgotinib 100 mg vs Placebo
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	955
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [18]
Method	Regression, Logistic
Parameter estimate	Difference in Response Rates
Point estimate	19
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.4
upper limit	24.6

Notes:

[18] - P-value was calculated from the logistic regression with treatment groups and stratification factors in the model.

Secondary: Change from Baseline in Modified Total Sharp Score (mTSS) at Week 24

End point title	Change from Baseline in Modified Total Sharp Score (mTSS) at Week 24[19]

End point description:

Participant`s radiographs of bilateral hands, wrists and feet are taken and evaluated through central

review using the mTSS method. The mTSS (range [0-448]) is defined as the erosion score (range [0-280]) plus the joint space narrowing (JSN) score (range [0-168]). An erosion score of 0 to 5 is given to each joint in the hands and wrists, and a score of 0 to 10 is given to each joint in the feet where 0 indicates no erosion while 5 or 10 indicates extensive loss of bone (maximum erosion). JSN is scored from 0 to 4, with 0 indicating normal or no narrowing and 4 indicating complete loss of joint space. The maximal TSS is 448. Negative change in value indicates improvement (less erosion of bone, normal joint spaces). Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 24

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The Baseline period arms for Placebo [Placebo to Filgotinib 200 mg, Placebo to Filgotinib 100 mg, and Placebo never received Filgotinib] were combined to present data for the total number of participants who received Placebo.

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Adalimumab	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	467	471	319	466
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline	32.47 (± 47.939)	36.70 (± 53.065)	34.82 (± 55.013)	31.60 (± 53.217)
Change at Week 24 (n=405, 404, 271, 351)	0.13 (± 0.937)	0.17 (± 0.905)	0.16 (± 0.948)	0.37 (± 1.417)

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo
Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	933
Analysis specification	Pre-specified
Analysis type	superiority[20]
P-value	< 0.001 [21]
Method	MMRM
Parameter estimate	Least Squares Mean Difference
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.43
upper limit	-0.12
Variability estimate	Standard error of the mean
Dispersion value	0.078

Notes:

[20] - LS-Mean, 95% CI, and P-value were provided from MMRM. Missing change scores were not imputed using the MMRM approach assuming an unstructured variance-covariance matrix for the repeated measures.
[21] - MMRM model included treatment, visit, treatment by visit, stratification factors, and baseline value as fixed effects, and subjects being the random effect.

Statistical analysis title	Filgotinib 100 mg vs Placebo

Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	937
Analysis specification	Pre-specified
Analysis type	superiority[22]
P-value	= 0.001 [23]
Method	MMRM
Parameter estimate	Least Squares Mean Difference
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.078

Notes:

[22] - LS-Mean, 95% CI, and P-value were provided from MMRM. Missing change scores were not imputed using the MMRM approach assuming an unstructured variance-covariance matrix for the repeated measures.

[23] - MMRM model included treatment, visit, treatment by visit, stratification factors, and baseline value as fixed effects, and subjects being the random effect.

Adverse events information

Timeframe for reporting adverse events:

First dose date up to last dose date (Maximum: 54 weeks) plus 30 days

Adverse event reporting additional description:

The Safety Analysis Set included all participants who received at least 1 dose of study drug. Treatment relatedness refers to study drug filgotinib, adalimumab and placebo to match, not other background treatment (MTX).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Filgotinib 200 mg

Reporting group description:

Participants were administered a filgotinib 200 mg tablet orally, once daily + a placebo to match (PTM) filgotinib 100 mg tablet orally, once daily + PTM adalimumab 40 mg subcutaneous (SC) injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 52.1 weeks.

Reporting group title	Filgotinib 100 mg

Reporting group description:

Participants were administered a filgotinib 100 mg tablet orally, once daily + a PTM filgotinib 200 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 52.1 weeks.

Reporting group title	Adalimumab

Reporting group description:

Participants were administered a PTM filgotinib 200 mg tablet orally, once daily + a PTM filgotinib 100 mg tablet orally, once daily + adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 52.1 weeks.

Reporting group title	Placebo to Filgotinib 200 mg

Reporting group description:

Participants in the placebo arm were administered a PTM filgotinib 200 mg tablet orally, once daily+ a PTM filgotinib 100 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 24 weeks. Then the participants in the placebo arm were rerandomized to filgotinib 200 mg and were administered a filgotinib 200 mg tablet orally, once daily + PTM filgotinib 100 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 28.1 weeks.

Reporting group title	Placebo to Filgotinib 100 mg

Reporting group description:

Participants in the placebo arm were administered a PTM filgotinib 200 mg tablet orally, once daily+ a PTM filgotinib 100 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 24 weeks. Then the participants in the placebo arm were rerandomized to filgotinib 100 mg and were administered a filgotinib 100 mg tablet orally, once daily + PTM filgotinib 200 mg tablet orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 28.1 weeks.

Reporting group title	Placebo

Reporting group description:

The Placebo arm included all participants who received placebo in the study. Participants were administered PTM filgotinib 200 mg tablets orally, once daily+ PTM filgotinib 100 mg tablets orally, once daily + PTM adalimumab 40 mg SC injection, once every 2 weeks in addition to a weekly stable dose of MTX, orally for median exposure of 24 weeks.

Serious adverse events	Filgotinib 200 mg	Filgotinib 100 mg	Adalimumab
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 475 (7.37%)	40 / 480 (8.33%)	22 / 325 (6.77%)
number of deaths (all causes)	3	1	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	1 / 325 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer stage I			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix carcinoma stage III			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Leiomyosarcoma metastatic			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Malignant glioma			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to liver			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Pancreatic carcinoma			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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

Prostate cancer			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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			
Deep vein thrombosis			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	1 / 325 (0.31%)
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	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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 artery occlusion			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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			
Metrorrhagia			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Prostatitis			

subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine haemorrhage			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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 haemorrhage			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	2 / 475 (0.42%)	0 / 480 (0.00%)	0 / 325 (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
Pulmonary embolism			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Alveolitis			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Bronchiectasis			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Organising pneumonia			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			

subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Respiratory failure			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Rheumatoid lung			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Vocal cord polyp			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	1 / 325 (0.31%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	1 / 325 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood creatinine increased			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Hip fracture			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	1 / 325 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Coronary artery restenosis			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Meniscus injury			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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

Road traffic accident			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scapula fracture			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Toxicity to various agents			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	1 / 325 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Angina unstable			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Cor pulmonale chronic			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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 tachycardia			

subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	1 / 325 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Ischaemic stroke			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 475 (0.00%)	2 / 480 (0.42%)	0 / 325 (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
Carotid artery stenosis			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	1 / 325 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiplegia			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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 and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Anaemia			

subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Febrile neutropenia			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Meniere's disease			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertigo			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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	1 / 475 (0.21%)	0 / 480 (0.00%)	1 / 325 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Macular fibrosis			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Vitreous opacities			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	0 / 475 (0.00%)	2 / 480 (0.42%)	0 / 325 (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 acute			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	1 / 325 (0.31%)
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	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Colitis			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Duodenal ulcer perforation			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Gastritis			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Gastrointestinal inflammation			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Mouth ulceration			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Obstructive pancreatitis			

subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peptic ulcer			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Stomatitis			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Vomiting			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	2 / 475 (0.42%)	1 / 480 (0.21%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Cholecystitis acute			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Skin ulcer			
subjects affected / exposed	1 / 475 (0.21%)	1 / 480 (0.21%)	0 / 325 (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
Angioedema			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pustular psoriasis			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	1 / 325 (0.31%)
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 and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 475 (0.21%)	1 / 480 (0.21%)	0 / 325 (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
Nephrolithiasis			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Prerenal failure			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cell dysplasia			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Musculoskeletal and connective tissue			

disorders			
Rheumatoid arthritis			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Foot deformity			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc disorder			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	1 / 325 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Limb asymmetry			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Osteonecrosis			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	1 / 325 (0.31%)
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			

Pneumonia			
subjects affected / exposed	4 / 475 (0.84%)	4 / 480 (0.83%)	3 / 325 (0.92%)
occurrences causally related to treatment / all	4 / 4	3 / 4	2 / 3
deaths causally related to treatment / all	2 / 2	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	2 / 475 (0.42%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 475 (0.21%)	1 / 480 (0.21%)	1 / 325 (0.31%)
occurrences causally related to treatment / all	2 / 2	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	1 / 325 (0.31%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	1 / 325 (0.31%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	2 / 475 (0.42%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 2	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 475 (0.21%)	1 / 480 (0.21%)	0 / 325 (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
Varicella			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Abscess limb			

subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Candida infection			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Gastroenteritis			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Helicobacter infection			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	1 / 325 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected skin ulcer			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective tenosynovitis			

subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	1 / 325 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Paronychia			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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	0 / 475 (0.00%)	0 / 480 (0.00%)	1 / 325 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia fungal			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pneumococcal			
subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	0 / 325 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Sepsis			

subjects affected / exposed	0 / 475 (0.00%)	0 / 480 (0.00%)	1 / 325 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Sinusitis			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Tooth abscess			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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			
Dehydration			
subjects affected / exposed	0 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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
Electrolyte imbalance			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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
Hypervitaminosis			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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 / 475 (0.00%)	1 / 480 (0.21%)	0 / 325 (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 acidosis			
subjects affected / exposed	1 / 475 (0.21%)	0 / 480 (0.00%)	0 / 325 (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

Serious adverse events	Placebo to Filgotinib	Placebo to Filgotinib	Placebo

	200 mg	100 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 190 (3.68%)	8 / 191 (4.19%)	21 / 475 (4.42%)
number of deaths (all causes)	1	1	2
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer stage I			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix carcinoma stage III			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leiomyosarcoma metastatic			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant glioma			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to liver			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Prostate cancer			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
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 leiomyoma			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 190 (0.53%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery occlusion			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 190 (0.53%)	0 / 191 (0.00%)	0 / 475 (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
Reproductive system and breast disorders			
Metrorrhagia			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatitis			

subjects affected / exposed	0 / 190 (0.00%)	1 / 191 (0.52%)	0 / 475 (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
Uterine haemorrhage			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal haemorrhage			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 190 (0.53%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Alveolitis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiectasis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organising pneumonia			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			

subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid lung			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vocal cord polyp			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
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			
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 190 (0.00%)	1 / 191 (0.52%)	0 / 475 (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
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood creatinine increased			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery restenosis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Road traffic accident			
subjects affected / exposed	1 / 190 (0.53%)	0 / 191 (0.00%)	0 / 475 (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
Scapula fracture			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cor pulmonale chronic			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			

subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
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 stroke			
subjects affected / exposed	1 / 190 (0.53%)	1 / 191 (0.52%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
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	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery stenosis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiplegia			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			

subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Meniere's disease			
subjects affected / exposed	0 / 190 (0.00%)	1 / 191 (0.52%)	0 / 475 (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
Vertigo			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Macular fibrosis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitreous opacities			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	0 / 190 (0.00%)	1 / 191 (0.52%)	0 / 475 (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	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer perforation			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth ulceration			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive pancreatitis			

subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peptic ulcer			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
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 acute			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Skin ulcer			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angioedema			
subjects affected / exposed	1 / 190 (0.53%)	0 / 191 (0.00%)	0 / 475 (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
Dermatitis			
subjects affected / exposed	1 / 190 (0.53%)	0 / 191 (0.00%)	0 / 475 (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
Pustular psoriasis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prerenal failure			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cell dysplasia			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Rheumatoid arthritis			
subjects affected / exposed	0 / 190 (0.00%)	1 / 191 (0.52%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc disorder			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	1 / 190 (0.53%)	0 / 191 (0.00%)	0 / 475 (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
Arthritis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb asymmetry			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Pneumonia			
subjects affected / exposed	1 / 190 (0.53%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella			
subjects affected / exposed	0 / 190 (0.00%)	1 / 191 (0.52%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Abscess limb			

subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 190 (0.00%)	1 / 191 (0.52%)	0 / 475 (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
Candida infection			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Helicobacter infection			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected skin ulcer			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective tenosynovitis			

subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paronychia			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia fungal			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pneumococcal			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	1 / 475 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth abscess			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrolyte imbalance			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypervitaminosis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic acidosis			
subjects affected / exposed	0 / 190 (0.00%)	0 / 191 (0.00%)	0 / 475 (0.00%)
occurrences causally related to treatment / all	0 / 0	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	Filgotinib 200 mg	Filgotinib 100 mg	Adalimumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	128 / 475 (26.95%)	142 / 480 (29.58%)	82 / 325 (25.23%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	17 / 475 (3.58%)	25 / 480 (5.21%)	21 / 325 (6.46%)
occurrences (all)	24	31	24
Aspartate aminotransferase increased			
subjects affected / exposed	12 / 475 (2.53%)	20 / 480 (4.17%)	17 / 325 (5.23%)
occurrences (all)	16	29	19
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	26 / 475 (5.47%)	16 / 480 (3.33%)	6 / 325 (1.85%)
occurrences (all)	30	19	6
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	43 / 475 (9.05%)	48 / 480 (10.00%)	24 / 325 (7.38%)
occurrences (all)	53	58	27
Upper respiratory tract infection			
subjects affected / exposed	41 / 475 (8.63%)	49 / 480 (10.21%)	21 / 325 (6.46%)
occurrences (all)	49	65	27
Urinary tract infection			
subjects affected / exposed	18 / 475 (3.79%)	19 / 480 (3.96%)	17 / 325 (5.23%)
occurrences (all)	21	21	20

Non-serious adverse events	Placebo to Filgotinib 200 mg	Placebo to Filgotinib 100 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 190 (18.95%)	23 / 191 (12.04%)	61 / 475 (12.84%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	7 / 190 (3.68%)	3 / 191 (1.57%)	11 / 475 (2.32%)
occurrences (all)	7	3	11
Aspartate aminotransferase increased			

subjects affected / exposed	8 / 190 (4.21%)	3 / 191 (1.57%)	9 / 475 (1.89%)
occurrences (all)	9	3	9
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 190 (2.11%)	1 / 191 (0.52%)	7 / 475 (1.47%)
occurrences (all)	4	1	7
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 190 (3.68%)	6 / 191 (3.14%)	25 / 475 (5.26%)
occurrences (all)	9	8	31
Upper respiratory tract infection			
subjects affected / exposed	8 / 190 (4.21%)	6 / 191 (3.14%)	14 / 475 (2.95%)
occurrences (all)	10	6	16
Urinary tract infection			
subjects affected / exposed	10 / 190 (5.26%)	8 / 191 (4.19%)	6 / 475 (1.26%)
occurrences (all)	10	8	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 July 2016	• Terminology for the Open Label Extension study was changed to long-term extension (LTE) study • Updated study procedures to collect body weight at all study visits • Added urine biomarker samples as an exploratory endpoint • Updated study procedures to include Treatment Satisfaction Questionnaire for Medication (TSQM) collection at Day 1 and Week 12, 24, 36, and 52 visits. • Clarified eligibility criteria as needed • Updated Study Procedures, to reflect global protocol changes in study procedures and time points • Updated the Prior and Concomitant Medications section to clarify documentation of prior medications and restriction window on injectable corticosteroids • Updated to stipulate that viably frozen peripheral blood mononuclear cells and leukocyte subset samples would be drawn in the US and Canada only; removed peripheral blood mononuclear cell substudy • Clarified that the magnetic resonance imaging (MRI) substudy would be performed postrandomization within 7 days of first dose and at Week 12 within ± 7 days • Clarified that radiographs performed after randomization could be done ± 7 days of the scheduled visit • Added carotid artery ultrasound substudy at selected sites, when available • Updated Criteria for Interruption or Discontinuation of Study Treatment, to align across protocols

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported