



Clinical trial results:

A Randomized, Double-Blind, Placebo-Controlled, Multicenter, Phase 3 Study to Assess the Efficacy and Safety of Filgotinib Administered for 24 Weeks in Combination with Conventional Synthetic Disease-Modifying Anti-Rheumatic Drug(s) (csDMARDs) to Subjects with Moderately to Severely Active Rheumatoid Arthritis Who Have an Inadequate Response to Biologic DMARD(s) Treatment

Summary

EudraCT number	2016-000569-21
Trial protocol	BE GB DE FR HU ES PL NL
Global end of trial date	26 June 2018

Results information

Result version number	v1
This version publication date	04 July 2019
First version publication date	04 July 2019

Trial information

Trial identification

Sponsor protocol code	GS-US-417-0302
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02873936
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	26 June 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 March 2018
Global end of trial reached?	Yes
Global end of trial date	26 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the effects of filgotinib versus placebo for the treatment of signs and symptoms of rheumatoid arthritis (RA) as measured by the proportion 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:

All participants continued to receive a stable dose of a permitted protocol-specified conventional synthetic disease-modifying antirheumatic drug (csDMARD(s)) (methotrexate, hydroxychloroquine, sulfasalazine, or leflunomide).

Evidence for comparator: -

Actual start date of recruitment	27 July 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 19
Country: Number of subjects enrolled	Spain: 16
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Germany: 15
Country: Number of subjects enrolled	Hungary: 16
Country: Number of subjects enrolled	United States: 255
Country: Number of subjects enrolled	Japan: 40

Country: Number of subjects enrolled	Mexico: 30
Country: Number of subjects enrolled	Argentina: 12
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	Australia: 4
Country: Number of subjects enrolled	Israel: 3
Country: Number of subjects enrolled	Switzerland: 2
Worldwide total number of subjects	449
EEA total number of subjects	98

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)	336
From 65 to 84 years	113
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Argentina, Australia, Europe, Israel, Japan, Mexico, South Korea, and the United States. The first participant was screened on 27 July 2016. The last study visit occurred on 26 June 2018.

Pre-assignment

Screening details:

688 participants were screened.

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:

Filgotinib 200 mg tablet + placebo to match (PTM) filgotinib 100 mg tablet once daily + a stable dose of permitted csDMARDs for up to 24 weeks

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

Dosage and administration details:

200 mg tablet administered once daily

Investigational medicinal product name	Placebo
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

Arm title	Filgotinib 100 mg
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Arm description:

Filgotinib 100 mg tablet + PTM filgotinib 200 mg tablet once daily + a stable dose of permitted csDMARDs for up to 24 weeks

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

Dosage and administration details:

100 mg tablet administered once daily

Investigational medicinal product name	Placebo
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	
Arm title	Placebo

Arm description:

PTM filgotinib 200 mg tablet + PTM filgotinib 100 mg tablet once daily + a stable dose of permitted csDMARDs for up to 24 weeks

Arm type	Placebo
Investigational medicinal product name	Placebo
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	Placebo
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

Number of subjects in period 1^[1]	Filgotinib 200 mg	Filgotinib 100 mg	Placebo
Started	147	153	148
Completed	135	130	116
Not completed	12	23	32
Withdrew Consent	4	11	20
Adverse Event	3	5	3
Non-Compliance with Study Drug	1	-	1
Investigator's Discretion	3	5	4
Protocol Violation	-	1	3
Lost to follow-up	1	1	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 1 participant who was randomized but not treated is not included in the subject disposition table.

Baseline characteristics

Reporting groups

Reporting group title	Filgotinib 200 mg
Reporting group description: Filgotinib 200 mg tablet + placebo to match (PTM) filgotinib 100 mg tablet once daily + a stable dose of permitted csDMARDs for up to 24 weeks	
Reporting group title	Filgotinib 100 mg
Reporting group description: Filgotinib 100 mg tablet + PTM filgotinib 200 mg tablet once daily + a stable dose of permitted csDMARDs for up to 24 weeks	
Reporting group title	Placebo
Reporting group description: PTM filgotinib 200 mg tablet + PTM filgotinib 100 mg tablet once daily + a stable dose of permitted csDMARDs for up to 24 weeks	

Reporting group values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo
Number of subjects	147	153	148
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	56	55	56
standard deviation	± 12.5	± 12.0	± 12.1
Gender categorical			
Units: Subjects			
Female	120	119	121
Male	27	34	27
Race			
Units: Subjects			
American Indian or Alaska Native	7	9	10
Asian	15	20	15
Black or African American	14	12	21
White	110	109	97
Other	1	3	2
Not Permitted	0	0	3
Ethnicity			
Units: Subjects			
Hispanic or Latino	26	40	41
Not Hispanic or Latino	120	112	107
Not Permitted	1	1	0

Reporting group values	Total		
Number of subjects	448		
Age categorical			
Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	360		
Male	88		
Race Units: Subjects			
American Indian or Alaska Native	26		
Asian	50		
Black or African American	47		
White	316		
Other	6		
Not Permitted	3		
Ethnicity Units: Subjects			
Hispanic or Latino	107		
Not Hispanic or Latino	339		
Not Permitted	2		

End points

End points reporting groups

Reporting group title	Filgotinib 200 mg
Reporting group description: Filgotinib 200 mg tablet + placebo to match (PTM) filgotinib 100 mg tablet once daily + a stable dose of permitted csDMARDs for up to 24 weeks	
Reporting group title	Filgotinib 100 mg
Reporting group description: Filgotinib 100 mg tablet + PTM filgotinib 200 mg tablet once daily + a stable dose of permitted csDMARDs for up to 24 weeks	
Reporting group title	Placebo
Reporting group description: PTM filgotinib 200 mg tablet + PTM filgotinib 100 mg tablet once daily + a stable dose of permitted csDMARDs for up to 24 weeks	

Primary: Percentage of Participants who Achieve an American College of Rheumatology (ACR) 20% Improvement (ACR20) Response at Week 12 using the Full Analysis Set

End point title	Percentage of Participants who Achieve an American College of Rheumatology (ACR) 20% Improvement (ACR20) Response at Week 12 using the Full Analysis Set
End point description: ACR20 response was defined as having $\geq 20\%$ improvement from baseline in tender joint count based on 68 joints (TJC68), $\geq 20\%$ improvement from baseline in swollen joint count based on 66 joints (SJC66), and $\geq 20\%$ improvement in at least 3 of the following 5 criteria: Physician's Global Assessment of Disease Activity (PGA), Subject's Global Assessment of Disease Activity (SGA), participant's pain assessment, Health Assessment Questionnaire - Disability Index (HAQ-DI) score, and high-sensitivity C-reactive protein (hsCRP). Full Analysis Set included all randomized participants who received at least 1 dose of study drug. Participants with missing outcomes were set as non-responders. For statistical analyses, the hierarchical testing procedure was performed to control the overall type I error rate for the primary and key secondary endpoints.	
End point type	Primary
End point timeframe: Week 12	

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	147	153	148	
Units: percentage of participants				
number (confidence interval 95%)	66.0 (58.0 to 74.0)	57.5 (49.4 to 65.7)	31.1 (23.3 to 38.9)	

Statistical analyses

Statistical analysis title	ACR20 - Filgotinib 200 mg vs Placebo
Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[1]
Method	Regression, Logistic
Parameter estimate	Difference in Response Rates
Point estimate	34.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	23.5
upper limit	46.3

Notes:

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

Statistical analysis title	ACR20 - Filgotinib 100 mg vs Placebo
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[2]
Method	Regression, Logistic
Parameter estimate	Difference in Response Rates
Point estimate	26.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	15
upper limit	37.9

Notes:

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

Secondary: Percentage of Participants who Achieve Disease Activity Score 28 C-Reactive Protein (DAS28(CRP)) ≤ 3.2 at Week 12 using the Full Analysis Set

End point title	Percentage of Participants who Achieve Disease Activity Score 28 C-Reactive Protein (DAS28(CRP)) ≤ 3.2 at Week 12 using the Full Analysis Set
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End point description:

DAS28(CRP) is a measure of the participant's disease activity calculated using the tender joint counts (28 joints), swollen joint counts (28 joints), SGA, and hsCRP for a total possible score of 1 to 9.4. Higher values indicate more severe disease activity. Participants in the Full Analysis Set were analyzed. Participants with missing outcomes were set as non-responders. For statistical analyses, the hierarchical testing procedure was performed to control the overall type I error rate for the primary and key secondary endpoints.

End point type	Secondary
End point timeframe:	
Week 12	

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	147	153	148	
Units: percentage of participants				
number (confidence interval 95%)	40.8 (32.5 to 49.1)	37.3 (29.3 to 45.2)	15.5 (9.4 to 21.7)	

Statistical analyses

Statistical analysis title	DAS28(CRP) Response - Filgotinib 200 mg vs Placebo
Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[3]
Method	Regression, Logistic
Parameter estimate	Difference in Response Rates
Point estimate	25.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.7
upper limit	35.8

Notes:

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

Statistical analysis title	DAS28(CRP) Response - Filgotinib 100 mg vs Placebo
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[4]
Method	Regression, Logistic
Parameter estimate	Difference in Response Rates
Point estimate	21.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.4
upper limit	32

Notes:

[4] - 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
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End point description:

HAQ-DI is a self-reported tool used to assess the ability to perform tasks in 8 functional categories: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and common daily activities. Responses in each functional category were collected as 0 (without any difficulty) to 3 (unable to do a task in that area). The HAQ-DI score was calculated as the average of the scores of the 8 functional areas and ranges from 0 (no disability) to 3 (completely disabled), when 6 or more categories are non-missing. Participants in the Full Analysis Set with available data were analyzed. For statistical analyses, the hierarchical testing procedure was performed to control the overall type I error rate for the primary and key secondary endpoints.

End point type	Secondary
End point timeframe:	
Week 12	

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	137	140	129	
Units: units on a scale				
arithmetic mean (standard deviation)	-0.55 (± 0.590)	-0.48 (± 0.602)	-0.23 (± 0.547)	

Statistical analyses

Statistical analysis title	HAQ-DI Score - Filgotinib 200 mg vs Placebo
Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	other ^[5]
P-value	< 0.001 ^[6]
Method	Mixed models analysis
Parameter estimate	LSM of Treatment Difference
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	-0.19
Variability estimate	Standard error of the mean
Dispersion value	0.066

Notes:

[5] - The mixed-effects model for repeated measures (MMRM) included treatment, visit (as categorical), treatment by visit, stratification factors, and baseline value as fixed effects, and participants being the random effect.

[6] - Least square mean (LSM), 95% CI, and P-value were calculated using the MMRM. Missing change

scores were not imputed using the MMRM approach assuming an unstructured variance-covariance matrix for the repeated measures.

Statistical analysis title	HAQ-DI Score - Filgotinib 100 mg vs Placebo
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	269
Analysis specification	Pre-specified
Analysis type	other ^[7]
P-value	< 0.001 ^[8]
Method	Mixed models analysis
Parameter estimate	LSM of Treatment Difference
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	-0.14
Variability estimate	Standard error of the mean
Dispersion value	0.065

Notes:

[7] - The MMRM included treatment, visit (as categorical), treatment by visit, stratification factors, and baseline value as fixed effects, and participants being the random effect.

[8] - LSM, 95% CI, and P-value were calculated using the MMRM. Missing change scores were not imputed using the MMRM approach assuming an unstructured variance-covariance matrix for the repeated measures.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: Enrollment up to Week 24 plus 30 days; All-Cause Mortality: Enrollment up to Posttreatment Week 4

Adverse event reporting additional description:

Safety Analysis Set included all participants who received at least 1 dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Filgotinib 200 mg
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Reporting group description:

Filgotinib 200 mg tablet + PTM filgotinib 100 mg tablet once daily + a stable dose of permitted csDMARDs for up to 24 weeks

Reporting group title	Filgotinib 100 mg
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Reporting group description:

Filgotinib 100 mg tablet + PTM filgotinib 200 mg tablet once daily + a stable dose of permitted csDMARDs for up to 24 weeks

Reporting group title	Placebo
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Reporting group description:

PTM filgotinib 200 mg tablet + PTM filgotinib 100 mg tablet once daily + a stable dose of permitted csDMARDs for up to 24 weeks

Serious adverse events	Filgotinib 200 mg	Filgotinib 100 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 147 (4.08%)	8 / 153 (5.23%)	5 / 148 (3.38%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 147 (0.68%)	0 / 153 (0.00%)	0 / 148 (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
Laceration			
subjects affected / exposed	1 / 147 (0.68%)	0 / 153 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			

subjects affected / exposed	0 / 147 (0.00%)	0 / 153 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	1 / 147 (0.68%)	0 / 153 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 147 (0.00%)	0 / 153 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial ischaemia			
subjects affected / exposed	0 / 147 (0.00%)	1 / 153 (0.65%)	0 / 148 (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			
Anaemia			
subjects affected / exposed	0 / 147 (0.00%)	1 / 153 (0.65%)	0 / 148 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 147 (0.00%)	0 / 153 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 147 (0.00%)	0 / 153 (0.00%)	1 / 148 (0.68%)
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			
Vertigo			

subjects affected / exposed	1 / 147 (0.68%)	0 / 153 (0.00%)	0 / 148 (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			
Diarrhoea			
subjects affected / exposed	1 / 147 (0.68%)	0 / 153 (0.00%)	0 / 148 (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
Nausea			
subjects affected / exposed	0 / 147 (0.00%)	0 / 153 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 147 (0.00%)	0 / 153 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterine haemorrhage			
subjects affected / exposed	1 / 147 (0.68%)	0 / 153 (0.00%)	0 / 148 (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, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 147 (0.00%)	0 / 153 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	1 / 147 (0.68%)	0 / 153 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			

subjects affected / exposed	0 / 147 (0.00%)	1 / 153 (0.65%)	0 / 148 (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			
Bursitis			
subjects affected / exposed	1 / 147 (0.68%)	0 / 153 (0.00%)	0 / 148 (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
Lumbar spinal stenosis			
subjects affected / exposed	0 / 147 (0.00%)	1 / 153 (0.65%)	0 / 148 (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
Osteitis			
subjects affected / exposed	0 / 147 (0.00%)	1 / 153 (0.65%)	0 / 148 (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
Rheumatoid arthritis			
subjects affected / exposed	0 / 147 (0.00%)	0 / 153 (0.00%)	1 / 148 (0.68%)
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			
Gastroenteritis			
subjects affected / exposed	0 / 147 (0.00%)	0 / 153 (0.00%)	2 / 148 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess oral			
subjects affected / exposed	0 / 147 (0.00%)	1 / 153 (0.65%)	0 / 148 (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
Bronchitis			
subjects affected / exposed	0 / 147 (0.00%)	1 / 153 (0.65%)	0 / 148 (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

Cellulitis			
subjects affected / exposed	1 / 147 (0.68%)	0 / 153 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder empyema			
subjects affected / exposed	0 / 147 (0.00%)	1 / 153 (0.65%)	0 / 148 (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
Vulval abscess			
subjects affected / exposed	0 / 147 (0.00%)	1 / 153 (0.65%)	0 / 148 (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	1 / 147 (0.68%)	0 / 153 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 147 (0.00%)	0 / 153 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lactic acidosis			
subjects affected / exposed	1 / 147 (0.68%)	0 / 153 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Filgotinib 200 mg	Filgotinib 100 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 147 (26.53%)	35 / 153 (22.88%)	31 / 148 (20.95%)
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 147 (5.44%)	9 / 153 (5.88%)	2 / 148 (1.35%)
occurrences (all)	8	11	2

Gastrointestinal disorders			
Nausea			
subjects affected / exposed	7 / 147 (4.76%)	8 / 153 (5.23%)	5 / 148 (3.38%)
occurrences (all)	9	8	5
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	2 / 147 (1.36%)	2 / 153 (1.31%)	8 / 148 (5.41%)
occurrences (all)	2	2	11
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	15 / 147 (10.20%)	9 / 153 (5.88%)	7 / 148 (4.73%)
occurrences (all)	15	11	7
Upper respiratory tract infection			
subjects affected / exposed	8 / 147 (5.44%)	9 / 153 (5.88%)	6 / 148 (4.05%)
occurrences (all)	9	9	6
Bronchitis			
subjects affected / exposed	8 / 147 (5.44%)	3 / 153 (1.96%)	8 / 148 (5.41%)
occurrences (all)	9	5	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 July 2016	<ul style="list-style-type: none">• Updated to reflect the removal of radiologic assessments (including removal of modified Total Sharp Score [mTSS] objectives as a measure of joint structural damage derived from x-rays)• Added urine biomarker samples as an exploratory endpoint• Updated study procedures to collect body weight at all study visits• Updated study procedures to include Treatment Satisfaction Questionnaire for Medication (TSQM) collection at several study visits• Added a carotid artery ultrasound substudy• Added an assessment of quantitative immunoglobulin (Ig) at Day 1 and Week 24 (Early Termination)• Added assessments of hemoglobin A1c (HbA1c), leptin, low-density lipoprotein (LDL) particle, homocysteine, and Apo A1/B for subjects participating in the carotid artery ultrasound substudy• Removed peripheral blood mononuclear cell biomarker sampling• Clarified criteria for interruption of study drugs• Updated the definition of postmenopausal females

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported