Clinical trial results:
A Randomized, Double-blind, Placebo-controlled, Multicenter, Phase II Study to Assess the Efficacy and Safety of Filgotinib Administered for 12 Weeks to Subjects With Active Ankylosing Spondylitis

Summary

EudraCT number	2016-003636-21
Trial protocol	EE CZ ES BG BE
Global end of trial date	02 July 2018

Results information

Result version number	v1 (current)
This version publication date	24 April 2019
First version publication date	24 April 2019

Trial information

Trial identification

Sponsor protocol code	GLPG0634-CL-223

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03117270
WHO universal trial number (UTN)	-
Other trial identifiers	Study Acronym: TORTUGA

Notes:

Sponsors

Sponsor organisation name	Galapagos NV
Sponsor organisation address	Generaal De Wittelaan L11 A3, Mechelen, Belgium, 2800
Public contact	Clinical Trial Information Desk, Galapagos NV, +32 15342 900, rd@glpg.com
Scientific contact	Clinical Trial Information Desk, Galapagos NV, +32 15342 900, rd@glpg.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	31 January 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 July 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Objective:
- Evaluate the effect of filgotinib 200 mg once daily compared with placebo once daily on the signs and symptoms of ankylosing spondylitis (AS), as assessed by the ankylosing spondylitis disease activity score (ASDAS) at Week 12

Secondary Objectives:
- Evaluate the effect of filgotinib 200 mg compared with placebo on:
  - The signs and symptoms of AS
  - Physical function
  - Spinal mobility
  - Spinal and sacroiliac joint inflammation
  - Enthesitis
  - Quality of life
- Evaluate the safety and tolerability of filgotinib 200 mg

Protection of trial subjects:

This study was conducted in accordance with recognized international scientific and ethical standards including, but not limited to, the International Council for Harmonisation (ICH) guideline for Good Clinical Practice (GCP) (Sections 7.6 and 8.2), and the original principles embodied in the Declaration of Helsinki. These standards are consistent with the requirements of the European Community Directive 2001/20/EC. For Ukraine, standards were in accordance with Ukraine Guidance "Medicinal Products. Good clinical practice ССТ-Н МОЗУ 42-7.0:2008" approved by Ministry of Health Order of 16 February 2009 No. 95 and with consideration of requirements of Directive 2001/20/EC.
Investigators (or designee[s]) were responsible for obtaining written informed consent from each individual who participated in this study after adequate explanation of the aims, methods, objectives, and potential hazards of the study and before undertaking any study-related procedures. Participants were informed that they were completely free to refuse to enter the study or to withdraw from it at any time for any reason.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 March 2017
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	Ukraine: 64
Country: Number of subjects enrolled	Poland: 12
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	Belgium: 2

Country: Number of subjects enrolled	Bulgaria: 24
Country: Number of subjects enrolled	Czech Republic: 6
Country: Number of subjects enrolled	Estonia: 2
Worldwide total number of subjects	116
EEA total number of subjects	52

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)	115
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Europe. The first participant was screened on 07 March 2017. The last study visit occurred on 02 July 2018.

Pre-assignment

Screening details:

263 subjects were screened, of whom 116 were randomized and received at least 1 dose of study drug.

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, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Filgotinib 200 mg

Arm description:

Participants received filgotinib 200 mg tablet orally once daily for 12 weeks.

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

Dosage and administration details:

Participants received filgotinib 200 mg tablet orally once daily for 12 weeks.

Arm title	Placebo

Arm description:

Participants received placebo to match filgotinib tablet orally once daily for 12 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:

Participants received placebo to match filgotinib tablet orally once daily for 12 weeks.

Number of subjects in period 1	Filgotinib 200 mg	Placebo
Started	58	58
Completed	55	52
Not completed	3	6
Consent withdrawn by subject	-	2
Adverse event, non-fatal	1	-
Protocol violation	-	1
Lost to follow-up	2	2
Lack of efficacy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Filgotinib 200 mg
Reporting group description:	
Participants received filgotinib 200 mg tablet orally once daily for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo to match filgotinib tablet orally once daily for 12 weeks.	

Reporting group values	Filgotinib 200 mg	Placebo	Total
Number of subjects	58	58	116
Age categorical Units: Subjects			
< 40 years	26	25	51
40 to 50 years	19	24	43
50 to 65 years	12	9	21
> 65 years	1	0	1
Age continuous Units: years			
median	45	43	
full range (min-max)	21 to 73	21 to 64	-
Gender categorical Units: Subjects			
Female	13	17	30
Male	45	41	86
Race Units: Subjects			
White	58	58	116
Body Mass Index Units: kg/m²			
median	25.17	25.74	
full range (min-max)	18.22 to 37.90	16.49 to 43.82	-

End points

End points reporting groups

Reporting group title	Filgotinib 200 mg
Reporting group description:	
Participants received filgotinib 200 mg tablet orally once daily for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo to match filgotinib tablet orally once daily for 12 weeks.	

Primary: Change From Baseline in the Ankylosing Spondylitis Disease Activity Score (ASDAS) at Week 12

End point title	Change From Baseline in the Ankylosing Spondylitis Disease Activity Score (ASDAS) at Week 12

End point description:

The ASDAS is a composite score of 5 domains: total back pain rated on a 0 to 10 numeric rating scale (NRS) (0 = not severe and 10 = very severe); patient's global assessment of disease activity (PGADA) rated on a 0 to 10 NRS (0 = not active and 10 = very active); peripheral joint pain and/or swelling rated on a 0 to 10 NRS (0 = not severe and 10 = very severe); duration of morning stiffness rated on a 0 to 10 NRS (0 = 0 hours and 10 = 2 or more hours); high-sensitivity C-reactive protein (hsCRP) in mg/L (if hsCRP was nonmissing and < 2 mg/L, 2 mg/L was used in calculation).
ASDAS = 0.121 × (total back pain) + 0.110 × (PGADA) + 0.073 × (peripheral joint pain and/or swelling) + 0.058 × (duration of morning stiffness) + 0.579 × Ln(max[hsCRP, 2] + 1).
The ASDAS has a continuous scale starting from 0 with no defined upper end. A higher score indicated higher disease activity.
The Full Analysis Set included all randomized participants who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Baseline, Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58[1]	58[2]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	4.2 (± 0.62)	4.2 (± 0.79)		
Change at Week 12	-1.5 (± 1.04)	-0.6 (± 0.82)		

Notes:

[1] - Missing values were imputed using the Last Observation Carried Forward (LOCF) method.

[2] - Missing values were imputed using the Last Observation Carried Forward (LOCF) method.

Statistical analyses

Statistical analysis title	Change in ASDAS at Week 12

Statistical analysis description:

Analysis of covariance (ANCOVA) model with factors for treatment, baseline value, and randomization stratification was used for the calculation of between-group p-value.

Comparison groups	Filgotinib 200 mg v Placebo

Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Least-Squares (LS) Mean Difference
Point estimate	-0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.17
upper limit	-0.53
Variability estimate	Standard error of the mean
Dispersion value	0.16

Secondary: Percentage of Participants Achieving Assessment of Spondylo Arthritis international Society (ASAS)20 Response at Week 12

End point title	Percentage of Participants Achieving Assessment of Spondylo Arthritis international Society (ASAS)20 Response at Week 12

End point description:

The ASAS20 response was defined as at least 20% improvement and at least 1-unit improvement in at least 3 out of 4 domains, and no worsening by at least 20% and at least 1 unit in the remaining domain. The 4 domains used were: PGADA rated on a 0 to 10 NRS (0 = not active and 10 = very active); patient's assessment of spinal pain (PASP) rated on a 0 to 10 NRS (0 = no pain and 10 = most severe pain); bath ankylosing spondylitis functional index (BASFI) that rated physical functioning on a 0 to 10 NRS (0 = easy and 10 = impossible); and morning stiffness intensity and duration rated on a 0 to 10 NRS (0 = not severe or 0 hours and 10 = very severe or ≥ 2 hours). The 95% confidence interval (CI) for response rate was computed using the Wilson method.
The participants in Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	58		
Units: percentage of participants				
number (confidence interval 95%)	75.9 (63.47 to 85.04)	39.7 (28.09 to 52.51)		

Statistical analyses

Statistical analysis title	ASAS20 Response Rate at Week 12

Statistical analysis description:

Cochran-Mantel-Haenszel test for general association, controlling for randomization stratification factors was used for the calculation of between-group p-value. 95% CI for the difference in response rate was computed using the Newcombe method.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	36.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.35
upper limit	50.97

Secondary: Percentage of Participants Achieving ASAS40 Response at Week 12

End point title	Percentage of Participants Achieving ASAS40 Response at Week 12

End point description:

The ASAS40 response was defined as at least 40% improvement and at least 2-unit improvement in at least 3 out of 4 domains, and no worsening at all in the remaining domain. The 4 domains used were: PGADA rated on a 0 to 10 NRS (0 = not active and 10 = very active); PASP rated on a 0 to 10 NRS (0 = no pain and 10 = most severe pain); BASFI that rated physical functioning on a 0 to 10 NRS (0 = easy and 10 = impossible); and morning stiffness intensity and duration rated on a 0 to 10 NRS (0 = not severe or 0 hours and 10 = very severe or ≥ 2 hours). The 95% CI for response rate was computed using the Wilson method.
The participants in Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	58		
Units: percentage of participants				
number (confidence interval 95%)	37.9 (26.56 to 50.80)	19.0 (10.93 to 30.85)		

Statistical analyses

Statistical analysis title	ASAS40 Response Rate at Week 12

Statistical analysis description:

Cochran-Mantel-Haenszel test for general association, controlling for randomization stratification factors was used for the calculation of between-group p-value. 95% CI for the difference in response rate was computed using the Newcombe method.

Comparison groups	Filgotinib 200 mg v Placebo

Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0189
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	18.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.52
upper limit	34.13

Secondary: Percentage of Participants Achieving ASAS5/6 Response at Week 12

End point title	Percentage of Participants Achieving ASAS5/6 Response at Week 12

End point description:

The ASAS5/6 response was defined as at least 20% improvement in at least 5 out of 6 domains. The 6 domains used were: PGADA rated on a 0 to 10 NRS (0 = not active and 10 = very active); PASP rated on a 0 to 10 NRS (0 = no pain and 10 = most severe pain); BASFI that rated physical functioning on a 0 to 10 NRS (0 = easy and 10 = impossible); morning stiffness intensity and duration rated on a 0 to 10 NRS (0 = not severe or 0 hours and 10 = very severe or ≥ 2 hours); lateral spinal flexion (measured in cm with higher value = improvement); and hsCRP (higher value = worsening). The 95% CI for response rate was computed using the Wilson method.
The participants in Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	58		
Units: percentage of participants				
number (confidence interval 95%)	58.6 (45.80 to 70.37)	20.7 (12.25 to 32.77)		

Statistical analyses

Statistical analysis title	ASAS5/6 Response Rate at Week 12

Statistical analysis description:

Cochran-Mantel-Haenszel test for general association, controlling for randomization stratification factors was used for the calculation of between-group p-value. 95% CI for the difference in response rate was computed using the Newcombe method.

Comparison groups	Filgotinib 200 mg v Placebo

Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	37.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.31
upper limit	52.4

Secondary: Percentage of Participants Achieving ASAS Partial Remission (ASASPR) Response at Week 12

End point title	Percentage of Participants Achieving ASAS Partial Remission (ASASPR) Response at Week 12

End point description:

The ASASPR response was defined as achieving a value of not above 2 in each of 4 domains. The 4 domains used were: PGADA rated on a 0 to 10 NRS (0 = not active and 10 = very active); PASP rated on a 0 to 10 NRS (0 = no pain and 10 = most severe pain); BASFI that rated physical functioning on a 0 to 10 NRS (0 = easy and 10 = impossible); and morning stiffness intensity and duration rated on a 0 to 10 NRS (0 = not severe or 0 hours and 10 = very severe or ≥ 2 hours). The 95% CI for response rate was computed using the Wilson method.
The participants in Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	58		
Units: percentage of participants				
number (confidence interval 95%)	12.1 (5.97 to 22.88)	3.4 (0.95 to 11.73)		

Statistical analyses

Statistical analysis title	ASASPR Response Rate at Week 12

Statistical analysis description:

Cochran-Mantel-Haenszel test for general association, controlling for randomization stratification factors was used for the calculation of between-group p-value. 95% CI for the difference in response rate was computed using the Newcombe method.

Comparison groups	Placebo v Filgotinib 200 mg

Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1028
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	8.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.66
upper limit	19.72

Secondary: Change From Baseline in the Tender Joint Count of 44 Joints (TJC44) at Week 12

End point title	Change From Baseline in the Tender Joint Count of 44 Joints (TJC44) at Week 12

End point description:

Each of the following 44 joints were evaluated for tenderness: 2 sternoclavicular joints (left and right); 2 acromioclavicular joints (left and right); 2 shoulder joints (left and right); 2 elbows (left and right); 2 wrists (left and right); 10 metacarpophalangeal joints (left and right); 10 proximal interphalangeal joints (hands) (left and right); 2 knees (left and right); 2 ankles (left and right); 10 metatarsophalangeal joints (left and right). The tender joint count was done by scoring the presence or absence of tenderness as assessed by pressure and joint manipulation on physical examination. Baseline value was the last non-missing value on or prior to first dose date of study drug. Missing values were imputed using the LOCF method.
The participants in Full Analysis Set with ≥ 1 tender joint at baseline were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	47		
Units: tender joints				
arithmetic mean (standard deviation)				
Baseline	5.2 (± 4.93)	4.0 (± 2.46)		
Change at Week 12	-2.9 (± 3.00)	-1.5 (± 2.49)		

Statistical analyses

Statistical analysis title	Change in TJC44 at Week 12

Statistical analysis description:

ANCOVA model with factors for treatment, baseline value, and randomization stratification was used for the calculation of between-group p-value.

Comparison groups	Filgotinib 200 mg v Placebo

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0849
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.68
upper limit	0.11
Variability estimate	Standard error of the mean
Dispersion value	0.45

Secondary: Change From Baseline in the Swollen Joint Count of 44 Joints (SJC44) at Week 12

End point title	Change From Baseline in the Swollen Joint Count of 44 Joints (SJC44) at Week 12

End point description:

Each of the following 44 joints were evaluated for swelling: 2 sternoclavicular joints (left and right); 2 acromioclavicular joints (left and right); 2 shoulder joints (left and right); 2 elbows (left and right); 2 wrists (left and right); 10 metacarpophalangeal joints (left and right); 10 proximal interphalangeal joints (hands) (left and right); 2 knees (left and right); 2 ankles (left and right); 10 metatarsophalangeal joints (left and right). Synovial fluid and/or soft tissue swelling, but not bony overgrowth, represented a positive result for swollen joint count. Baseline value was the last non-missing value on or prior to first dose date of study drug. Missing values were imputed using the LOCF method.
The participants in Full Analysis Set with ≥ 1 swollen joint at baseline were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	20		
Units: swollen joints				
arithmetic mean (standard deviation)				
Baseline	1.8 (± 1.82)	2.2 (± 1.54)		
Change at Week 12	-1.7 (± 1.88)	-1.8 (± 1.65)		

Statistical analyses

Statistical analysis title	Change in SJC44 at Week 12

Statistical analysis description:

ANCOVA model with factors for treatment, baseline value, and randomization stratification was used for the calculation of between-group p-value.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1779
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	0.15
Variability estimate	Standard error of the mean
Dispersion value	0.22

Secondary: Percentage of Participants Achieving Clinically Meaningful Improvement (CMI) (Decrease of ASDAS From Baseline ≥ 1.1) at Week 12

End point title	Percentage of Participants Achieving Clinically Meaningful Improvement (CMI) (Decrease of ASDAS From Baseline ≥ 1.1) at Week 12

End point description:

The CMI was defined as a decrease in ASDAS from baseline of ≥ 1.1 points. The ASDAS is a composite score of 5 domains: total back pain (0 to 10 NRS, 0 = not severe and 10 = very severe); PGADA (0 to 10 NRS, 0 = not active and 10 = very active); peripheral joint pain and/or swelling (0 to 10 NRS, 0 = not severe and 10 = very severe); duration of morning stiffness (0 to 10 NRS, 0 = 0 hours and 10 = 2 or more hours); hsCRP in mg/L.
ASDAS = 0.121 × (total back pain) + 0.110 × (PGADA) + 0.073 × (peripheral joint pain and/or swelling) + 0.058 × (duration of morning stiffness) + 0.579 × Ln(max[hsCRP, 2] + 1).
The ASDAS has a continuous scale starting from 0 with no defined upper end. A higher score indicated higher disease activity. The 95% CI for response rate was computed using the Wilson method.
The participants in Full Analysis Set with baseline ASDAS value ≥ 1.1 were analyzed.

End point type	Secondary

End point timeframe:

Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	58		
Units: percentage of participants				
number (confidence interval 95%)	65.5 (52.67 to 76.44)	25.9 (16.35 to 38.38)		

Statistical analyses

Statistical analysis title	CMI at Week 12

Statistical analysis description:

Cochran-Mantel-Haenszel test for general association, controlling for randomization stratification factors was used for the calculation of between-group p-value. 95% CI for the difference in response rate was computed using the Newcombe method.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	39.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.72
upper limit	54.14

Secondary: Percentage of Participants Achieving Major Improvement (MI) (Decrease of ASDAS From Baseline ≥ 2.0) at Week 12

End point title	Percentage of Participants Achieving Major Improvement (MI) (Decrease of ASDAS From Baseline ≥ 2.0) at Week 12

End point description:

The MI was defined as a decrease in ASDAS from baseline of ≥ 2.0 points. The ASDAS is a composite score of 5 domains: total back pain (0 to 10 NRS, 0 = not severe and 10 = very severe); PGADA (0 to 10 NRS, 0 = not active and 10 = very active); peripheral joint pain and/or swelling (0 to 10 NRS, 0 = not severe and 10 = very severe); duration of morning stiffness (0 to 10 NRS, 0 = 0 hours and 10 = 2 or more hours); hsCRP in mg/L.
ASDAS = 0.121 × (total back pain) + 0.110 × (PGADA) + 0.073 × (peripheral joint pain and/or swelling) + 0.058 × (duration of morning stiffness) + 0.579 × Ln(max[hsCRP, 2] + 1).
The ASDAS has a continuous scale starting from 0 with no defined upper end. A higher score indicated higher disease activity. The 95% CI for response rate was computed using the Wilson method.
The participants in Full Analysis Set with baseline ASDAS value ≥ 2.0 were analyzed.

End point type	Secondary

End point timeframe:

Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	58		
Units: percentage of participants				
number (confidence interval 95%)	32.8 (22.08 to 45.58)	1.7 (0.31 to 9.14)		

Statistical analyses

Statistical analysis title	MI at Week 12

Statistical analysis description:

Cochran-Mantel-Haenszel test for general association, controlling for randomization stratification factors was used for the calculation of between-group p-value. 95% CI for the difference in response rate was computed using the Newcombe method.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	31.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.04
upper limit	43.93

Secondary: Percentage of Participants Achieving Inactive Disease (ID) (ASDAS <1.3) at Week 12

End point title	Percentage of Participants Achieving Inactive Disease (ID) (ASDAS <1.3) at Week 12

End point description:

The ID was defined as an ASDAS value < 1.3. The ASDAS is a composite score of 5 domains: total back pain (0 to 10 NRS, 0 = not severe and 10 = very severe); PGADA (0 to 10 NRS, 0 = not active and 10 = very active); peripheral joint pain and/or swelling (0 to 10 NRS, 0 = not severe and 10 = very severe); duration of morning stiffness (0 to 10 NRS, 0 = 0 hours and 10 = 2 or more hours); hsCRP in mg/L.
ASDAS = 0.121 × (total back pain) + 0.110 × (PGADA) + 0.073 × (peripheral joint pain and/or swelling) + 0.058 × (duration of morning stiffness) + 0.579 × Ln(max[hsCRP, 2] + 1).
The ASDAS has a continuous scale starting from 0 with no defined upper end. A higher score indicated higher disease activity. The 95% CI for response rate was computed using the Wilson method.
The participants in Full Analysis Set with baseline ASDAS value ≥ 1.3 were analyzed.

End point type	Secondary

End point timeframe:

Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	58		
Units: percentage of participants				
number (confidence interval 95%)	5.2 (1.77 to 14.14)	0.0 (0.00 to 6.21)		

Statistical analyses

Statistical analysis title	ID at Week 12

Statistical analysis description:

Cochran-Mantel-Haenszel test for general association, controlling for randomization stratification factors was used for the calculation of between-group p-value. 95% CI for the difference in response rate was computed using the Newcombe method.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0921
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	5.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.91
upper limit	14.14

Secondary: Percentage of Participants Achieving Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) 50% Response (BASDAI50) at Week 12

End point title	Percentage of Participants Achieving Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) 50% Response (BASDAI50) at Week 12

End point description:

The BASDAI is a 6-item index (fatigue, spinal pain, peripheral arthritis, enthesitis, intensity and duration of morning stiffness) in which the items were rated on a 0 to 10 NRS (0 = none or 0 hour and 10 = very severe or ≥ 2 hours). The BASDAI total score = (Q1 + Q2 + Q3 + Q4 + [(Q5 + Q6)/2])/5. The BASDAI total score ranged from 0 to 10, with a higher score indicating more severe disease activity. The BASDAI50 response was defined as a decrease in BASDAI total score from baseline of ≥ 50%. The 95% CI for response rate was computed using the Wilson method.
The participants in Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	58		
Units: percentage of participants				
number (confidence interval 95%)	24.1 (14.96 to 36.53)	13.8 (7.16 to 24.93)		

Statistical analyses

Statistical analysis title	BASDAI50 Response Rate at Week 12

Statistical analysis description:

Cochran-Mantel-Haenszel test for general association, controlling for randomization stratification factors was used for the calculation of between-group p-value. 95% CI for the difference in response rate was computed using the Newcombe method.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1134
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	10.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.08
upper limit	24.4

Secondary: Percentage of Participants Achieving ≥ 2 Units Improvement in BASDAI Total Score From Baseline at Week 12

End point title	Percentage of Participants Achieving ≥ 2 Units Improvement in BASDAI Total Score From Baseline at Week 12

End point description:

The BASDAI is a 6-item index (fatigue, spinal pain, peripheral arthritis, enthesitis, intensity and duration of morning stiffness) in which the items were rated on a 0 to 10 NRS (0 = none or 0 hour and 10 = very severe or ≥ 2 hours). The BASDAI total score = (Q1 + Q2 + Q3 + Q4 + [(Q5 + Q6)/2])/5. The BASDAI total score ranged from 0 to 10, with a higher score indicating more severe disease activity. Percentage of participants achieving ≥ 2 units improvement in BASDAI from baseline at different time points was reported. The 95% CI for response rate was computed using the Wilson method.
The participants in Full Analysis Set with baseline BASDAI value ≥ 2 were analyzed.

End point type	Secondary

End point timeframe:

Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	58		
Units: percentage of participants				
number (confidence interval 95%)	58.6 (45.80 to 70.37)	31.0 (20.62 to 43.80)		

Statistical analyses

Statistical analysis title	BASDAI ≥ 2 units improvement at Week 12

Statistical analysis description:

Cochran-Mantel-Haenszel test for general association, controlling for randomization stratification factors was used for the calculation of between-group p-value. 95% CI for the difference in response rate was computed using the Newcombe method.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0025
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	27.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.49
upper limit	43.29

Secondary: Change From Baseline in BASDAI Total Score at Week 12

End point title	Change From Baseline in BASDAI Total Score at Week 12

End point description:

The BASDAI is a 6-item index (fatigue, spinal pain, peripheral arthritis, enthesitis, intensity and duration of morning stiffness) in which the items were rated on a 0 to 10 NRS (0 = none or 0 hour and 10 = very severe or ≥ 2 hours). The BASDAI total score = (Q1 + Q2 + Q3 + Q4 + [(Q5 + Q6)/2])/5. The BASDAI total score ranged from 0 to 10, with a higher score indicating more severe disease activity. Baseline value was the last non-missing value on or prior to first dose date of study drug. Missing values were imputed using the LOCF method.
The participants in Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	58		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	6.9 (± 1.16)	7.0 (± 1.33)		
Change at Week 12	-2.4 (± 2.01)	-1.4 (± 2.02)		

Statistical analyses

Statistical analysis title	Change in BASDAI Total Score at Week 12

Statistical analysis description:

ANCOVA model with factors for treatment, baseline value, and randomization stratification was used for the calculation of between-group p-value.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0052
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.69
upper limit	-0.3
Variability estimate	Standard error of the mean
Dispersion value	0.35

Secondary: Change From Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) Total Score at Week 12

End point title	Change From Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) Total Score at Week 12

End point description:

The BASFI total score was calculated as the average of 10 items (putting on socks, bending, reaching up, 2 items on getting up, standing, climbing steps, looking over shoulder, physical demanding activities, and full day's activities) that were rated on a 0 to 10 NRS (0 = easy and 10 = impossible). The BASFI total score ranged from 0 to 10, with a higher BASFI indicating a higher level of functional impairment. Baseline value was the last non-missing value on or prior to first dose date of study drug. Missing values were imputed using the LOCF method.
The participants in Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	58		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	7.0 (± 1.48)	6.9 (± 1.55)		
Change at Week 12	-2.4 (± 1.90)	-1.2 (± 1.88)		

Statistical analyses

Statistical analysis title	Change in BASFI Total Score at Week 12

Statistical analysis description:

ANCOVA model with factors for treatment, baseline value, and randomization stratification was used for the calculation of between-group p-value.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0015
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.78
upper limit	-0.43
Variability estimate	Standard error of the mean
Dispersion value	0.34

Secondary: Change From Baseline in Bath Ankylosing Spondylitis Metrology Index (BASMI) Total Score at Week 12

End point title	Change From Baseline in Bath Ankylosing Spondylitis Metrology Index (BASMI) Total Score at Week 12

End point description:

The BASMI total score was calculated as the average of 5 items (lateral spinal flexion, tragus-to-wall distance, lumber flexion [modified Schober], maximal intermalleolar distance, and cervical rotation). The unit for the first 4 items was 'cm', the unit for cervical rotation was 'degree'. Each item outcome was converted to score ranging from 0 to 10. The BASMI total score ranged from 0 to 10, with a higher score indicating a more severe limitation of movement due to ankylosing spondylitis. Baseline value was the last non-missing value on or prior to first dose date of study drug. Missing values were imputed using the LOCF method.
The participants in Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	58		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	5.1 (± 1.65)	5.3 (± 1.55)		
Change at Week 12	-0.8 (± 1.02)	-0.4 (± 0.70)		

Statistical analyses

Statistical analysis title	Change in BASMI Total Score at Week 12

Statistical analysis description:

ANCOVA model with factors for treatment, baseline value, and randomization stratification was used for

the calculation of between-group p-value.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0093
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.68
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.15

Secondary: Change From Baseline in Chest Expansion at Week 12

End point title	Change From Baseline in Chest Expansion at Week 12

End point description:

Chest expansion was measured as the difference between maximal inspiration and maximal forced expiration at the fourth intercostal space (in cm). The better of 2 assessments was reported. Baseline value was the last non-missing value on or prior to first dose date of study drug. Missing values were imputed using the LOCF method.
The participants in Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	58		
Units: cm				
arithmetic mean (standard deviation)				
Baseline	3.2 (± 2.12)	2.5 (± 1.55)		
Change at Week 12	0.2 (± 1.53)	0.0 (± 1.31)		

Statistical analyses

Statistical analysis title	Change in Chest Expansion at Week 12

Statistical analysis description:

ANCOVA model with factors for treatment, baseline value, and randomization stratification was used for the calculation of between-group p-value.

Comparison groups	Filgotinib 200 mg v Placebo

Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0254
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.07
upper limit	0.99
Variability estimate	Standard error of the mean
Dispersion value	0.23

Secondary: Change From Baseline in Occiput-To-Wall Distance at Week 12

End point title	Change From Baseline in Occiput-To-Wall Distance at Week 12

End point description:

Occiput-to-wall distance was measured as the distance (in cm) between the occiput and the wall with the participant's heels and back rested against the wall. The better of 2 assessments was reported. Baseline value was the last non-missing value on or prior to first dose date of study drug. Missing values were imputed using the LOCF method.
The participants in Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	58		
Units: cm				
arithmetic mean (standard deviation)				
Baseline	10.5 (± 8.31)	10.6 (± 7.99)		
Change at Week 12	-1.5 (± 3.80)	-1.0 (± 4.70)		

Statistical analyses

Statistical analysis title	Change in Occiput-To-Wall Distance at Week 12

Statistical analysis description:

ANCOVA model with factors for treatment, baseline value, and randomization stratification was used for the calculation of between-group p-value.

Comparison groups	Filgotinib 200 mg v Placebo

Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6141
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.85
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.74

Secondary: Change From Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Magnetic Resonance Imaging (MRI) Score at Week 12

End point title	Change From Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Magnetic Resonance Imaging (MRI) Score at Week 12

End point description:

The MRI images of the spine and sacroiliac joints were scored by a central reader using the SPARCC scoring system. Spine lesions were scored in all 23 spinal discovertebral units and total scores were provided. The maximal score for each discovertebral unit was 18, so the maximum SPARCC spine total score was 18 × 23 = 414. Sacroiliac joints were scored using 6 consecutive coronal slices from posterior to anterior. The maximal score for a single coronal slice was 12, so the maximum SPARCC sacroiliac joint total score was 12 × 6 = 72.
The participants in Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	53		
Units: units on a scale				
arithmetic mean (standard deviation)				
Spine Lesion: Baseline (n = 54, 52)	19.0 (± 19.71)	13.8 (± 19.93)		
Spine Lesion: Change at Week 12 (n = 47, 42)	-5.8 (± 11.13)	0.5 (± 7.47)		
Sacroiliac Joints: Baseline (n = 56, 53)	6.8 (± 10.89)	5.3 (± 6.93)		
Sacroiliac Joints: Change at Week 12 (n = 48, 42)	-3.5 (± 7.31)	0.1 (± 3.51)		

Statistical analyses

Statistical analysis title	Change in Spine Lesions SPARCC MRI at Week 12

Statistical analysis description:

ANCOVA model with factors for treatment, baseline value, and randomization stratification was used for the calculation of between-group p-value. Actual number of subjects included in this analysis = 89.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0066
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-5.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.75
upper limit	-1.62
Variability estimate	Standard error of the mean
Dispersion value	2.04

Statistical analysis title	Change in Sacroiliac Joints SPARCC MRI at Week 12

Statistical analysis description:

ANCOVA model with factors for treatment, baseline value, and randomization stratification was used for the calculation of between-group p-value. Actual number of subjects included in this analysis = 90.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	-0.46
Variability estimate	Standard error of the mean
Dispersion value	0.94

Secondary: Change From Baseline in Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) at Week 12

End point title	Change From Baseline in Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) at Week 12

End point description:

The MASES assessed the enthesitis disease status in 13 sites: costochondral 1 right/left, costochondral 7 right/left, spina iliaca anterior superior right/left, crista iliaca right/left, spina iliaca posterior right/left, processus spinosus L5, Achilles tendon, proximal insertion right/left. Each site was categorized as:

permanently not assessable, temporarily not assessable, asymptomatic, and tender only. Both "permanently not assessable" and "temporarily not assessable" were considered as missing assessments. For each non-missing site, a score of 1 was assigned for "tender only" and a score of 0 otherwise. The MASES was calculated as the sum of the scores of the 13 sites and ranged from 0 to 13. A higher score indicated a higher level of enthesitis.
Baseline value was the last non-missing value on or prior to first dose date of study drug. Missing values were imputed using the LOCF method.
The participants in Full Analysis Set with enthesitis at baseline were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	48		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	4.9 (± 2.79)	4.1 (± 2.86)		
Change at Week 12	-2.5 (± 2.79)	-2.2 (± 3.30)		

Statistical analyses

Statistical analysis title	Change in MASES at Week 12

Statistical analysis description:

ANCOVA model with factors for treatment, baseline value, and randomization stratification was used for the calculation of between-group p-value.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6012
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	0.48

Secondary: Change From Baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Total Score at Week 12

End point title	Change From Baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Total Score at Week 12

End point description:

The FACIT-Fatigue scale consisted of 13 items, each scored on a 5-point scale (0 = not at all to 4 = very much). The larger the participant's response to the questions (with the exception of 2 negatively stated that are scored reversely), the greater the fatigue. The sum of all responses resulted in the FACIT-Fatigue total score that ranged from 0 (worse score) to 52 (better score), with a higher score indicating a better quality of life. Baseline value was the last non-missing value on or prior to first dose date of study drug. Missing values were imputed using the LOCF method.
The participants in Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	58		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	24.1 (± 9.56)	24.2 (± 9.39)		
Change at Week 12	8.9 (± 8.86)	5.3 (± 10.94)		

Statistical analyses

Statistical analysis title	Change in FACIT-Fatigue Total Score at Week 12

Statistical analysis description:

ANCOVA model with factors for treatment, baseline value, and randomization stratification was used for the calculation of between-group p-value.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0422
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	3.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	6.75
Variability estimate	Standard error of the mean
Dispersion value	1.67

Secondary: Change From Baseline in 36-Item Short-Form Health Survey (SF-36) Summary Scores at Week 12

End point title	Change From Baseline in 36-Item Short-Form Health Survey (SF-36) Summary Scores at Week 12

End point description:

The SF-36 questionnaire consisted of 36 questions divided over 8 domains (physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health), with each domain score ranging from 0 (worst) to 100 (best), and higher scores reflecting better health-related functional status. Two summary scores (Mental Component Summary [MCS] and Physical Component Summary [PCS]) were computed based on weighted combinations of the 8 domain scores. The summary scores were standardized to score ranging from 0 to 100 using the SF-36's recalibration software, with higher scores indicated a better quality of life. Baseline value was the last non-missing value on or prior to first dose date of study drug. Missing values were imputed using the LOCF method. The participants in Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	58		
Units: units on a scale				
arithmetic mean (standard deviation)				
MCS: Baseline	43.7 (± 11.11)	44.2 (± 10.62)		
MCS: Change at Week 12	4.0 (± 7.05)	1.0 (± 9.83)		
PCS: Baseline	33.1 (± 5.63)	33.3 (± 5.79)		
PCS: Change at Week 12	8.4 (± 8.18)	3.8 (± 7.10)		

Statistical analyses

Statistical analysis title	Change in SF36-MCS at Week 12

Statistical analysis description:

ANCOVA model with factors for treatment, baseline value, and randomization stratification was used for the calculation of between-group p-value.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0703
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	5.29
Variability estimate	Standard error of the mean
Dispersion value	1.39

Statistical analysis title	Change in SF36-PCS at Week 12

Statistical analysis description:

ANCOVA model with factors for treatment, baseline value, and randomization stratification was used for the calculation of between-group p-value.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0008
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	4.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.88
upper limit	6.93
Variability estimate	Standard error of the mean
Dispersion value	1.27

Secondary: Change From Baseline in Ankylosing Spondylitis Quality of Life (ASQoL) Total Score at Week 12

End point title	Change From Baseline in Ankylosing Spondylitis Quality of Life (ASQoL) Total Score at Week 12

End point description:

The ASQoL consisted of 18 yes/no questions, with 1 point assigned for each 'yes' response. The ASQoL total score was the sum of the 18 items and ranged from 0 to 18. A lower score indicated a better quality of life. Baseline value was the last non-missing value on or prior to first dose date of study drug. Missing values were imputed using the LOCF method.
The participants in Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Filgotinib 200 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	58		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	12.8 (± 3.52)	11.8 (± 4.52)		
Change at Week 12	-4.8 (± 4.50)	-2.2 (± 3.97)		

Statistical analyses

Statistical analysis title	Change in ASQoL Total Score at Week 12

Statistical analysis description:

ANCOVA model with factors for treatment, baseline value, and randomization stratification was used for the calculation of between-group p-value.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0038
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.92
upper limit	-0.77
Variability estimate	Standard error of the mean
Dispersion value	0.79

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 12 plus 30 days

Adverse event reporting additional description:

The Safety Analysis Set included all participants who received at least 1 dose of study drug. The threshold of 3.4% applied for reporting non-serious adverse events corresponds to 2 subjects in a group.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Filgotinib 200 mg

Reporting group description:

Participants received filgotinib 200 mg tablet orally once daily for 12 weeks.

Reporting group title	Placebo

Reporting group description:

Participants received placebo to match filgotinib tablet orally once daily for 12 weeks.

Serious adverse events	Filgotinib 200 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 58 (1.72%)	0 / 58 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Infections and infestations			
Pneumonia bacterial			
subjects affected / exposed	1 / 58 (1.72%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3.4 %

Non-serious adverse events	Filgotinib 200 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 58 (31.03%)	18 / 58 (31.03%)	
Investigations			
Activated partial thromboplastin time prolonged			

subjects affected / exposed	2 / 58 (3.45%)	0 / 58 (0.00%)	
occurrences (all)	2	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 58 (0.00%)	3 / 58 (5.17%)	
occurrences (all)	0	3	
Neutrophil count decreased			
subjects affected / exposed	2 / 58 (3.45%)	1 / 58 (1.72%)	
occurrences (all)	3	1	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 58 (5.17%)	0 / 58 (0.00%)	
occurrences (all)	4	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 58 (0.00%)	2 / 58 (3.45%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 58 (0.00%)	2 / 58 (3.45%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	2 / 58 (3.45%)	3 / 58 (5.17%)	
occurrences (all)	2	3	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 58 (3.45%)	4 / 58 (6.90%)	
occurrences (all)	2	4	
Urinary tract infection			
subjects affected / exposed	1 / 58 (1.72%)	2 / 58 (3.45%)	
occurrences (all)	1	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2017	The benefit-risk assessment was updated based on clinical information regarding serious infections, lymphoma, and other malignancies, in accordance with the current version of the Investigator's Brochure (Edition 12, dated 22 May 2017). Also, an optional substudy was added, requiring a separate consent, in which urine and stool samples were to be collected for biomarker analysis. In addition, minor corrections, clarifications, and wording changes were made.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported