Clinical trial results:
A Phase 2, Randomized, Placebo-Controlled Trial Evaluating the Efficacy and Safety of Filgotinib in Subjects with Active Noninfectious Uveitis

Summary

EudraCT number	2017-001485-17
Trial protocol	GB
Global end of trial date	22 April 2021

Results information

Result version number	v1 (current)
This version publication date	11 January 2022
First version publication date	11 January 2022

Trial information

Trial identification

Sponsor protocol code	GS-US-432-4097

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03207815
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	22 April 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 December 2020
Global end of trial reached?	Yes
Global end of trial date	22 April 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy of filgotinib versus placebo for the treatment of the signs and symptoms of noninfectious uveitis as measured by the percentage of participants failing treatment for active noninfectious uveitis by Week 24.

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: -

Evidence for comparator: -

Actual start date of recruitment	26 July 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	Australia: 1
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 62
Worldwide total number of subjects	74
EEA total number of subjects	1

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	66
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States, the United Kingdom, Canada, Australia, Germany, Israel, and New Zealand. The first participant was screened on 26 July 2017. The last study visit occurred on 22 April 2021.

Pre-assignment

Screening details:

116 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

Arm description:

Participants received filgotinib 200 milligrams (mg) tablet orally, once daily for up to 52 weeks along with a standardized prednisone burst of 60 mg/day at Day 1/Baseline followed by a protocol-defined mandatory taper schedule up to Week 15.

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	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

60 mg administered once on Day 1/Baseline

Arm title	Placebo

Arm description:

Participants received placebo to match filgotinib tablet orally, once daily for up to 52 weeks along with a standardized prednisone burst of 60 mg/day at Day 1/Baseline followed by a protocol-defined mandatory taper schedule up to Week 15.

Arm type	Placebo
Investigational medicinal product name	Placebo to match filgotinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details: Administered once daily	
Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

60 mg administered once on Day 1/Baseline

Number of subjects in period 1[1]	Filgotinib	Placebo
Started	37	35
Completed	30	29
Not completed	7	6
Withdrew Consent	1	-
Adverse Event	1	2
Investigator's Discretion	1	1
Pregnancy/Partner Pregnancy	1	-
Protocol Violation	2	-
Lost to follow-up	1	2
Lack of efficacy	-	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: 2 participants who were enrolled but not treated were not included in the disposition table.

Baseline characteristics

Reporting groups	
Reporting group title	Filgotinib
Reporting group description:	
Participants received filgotinib 200 milligrams (mg) tablet orally, once daily for up to 52 weeks along with a standardized prednisone burst of 60 mg/day at Day 1/Baseline followed by a protocol-defined mandatory taper schedule up to Week 15.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo to match filgotinib tablet orally, once daily for up to 52 weeks along with a standardized prednisone burst of 60 mg/day at Day 1/Baseline followed by a protocol-defined mandatory taper schedule up to Week 15.	

Reporting group values	Filgotinib	Placebo	Total
Number of subjects	37	35	72
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	48	43	
standard deviation	± 15.1	± 15.7	-
Gender categorical Units: Subjects			
Female	23	20	43
Male	14	15	29
Race Units: Subjects			
Asian	4	0	4
Black or African American	2	8	10
Native Hawaiian or Pacific Islander	1	0	1
White	29	26	55
Other	1	1	2
Ethnicity			
Not Permitted = local regulators did not allow collection of ethnicity information.			
Units: Subjects			
Hispanic or Latino	4	10	14
Not Hispanic or Latino	32	25	57
Not Permitted	1	0	1

End points

End points reporting groups

Reporting group title	Filgotinib
Reporting group description:	
Participants received filgotinib 200 milligrams (mg) tablet orally, once daily for up to 52 weeks along with a standardized prednisone burst of 60 mg/day at Day 1/Baseline followed by a protocol-defined mandatory taper schedule up to Week 15.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo to match filgotinib tablet orally, once daily for up to 52 weeks along with a standardized prednisone burst of 60 mg/day at Day 1/Baseline followed by a protocol-defined mandatory taper schedule up to Week 15.	

Primary: Percentage of Participants Failing Treatment for Active NonInfectious Uveitis by Week 24

End point title	Percentage of Participants Failing Treatment for Active NonInfectious Uveitis by Week 24
End point description:	
Treatment failure was a participant meeting at least 1 of these criteria in at least 1 eye: New active, inflammatory lesions relative to Day 1/Baseline (all visits starting Wk 6); Inability to achieve ≤Grade 0.5+ (at Wk 6)/2-step increase (change of Grade 0 to Grade 2+/Grade 0.5+ to Grade 3+) (all visits after Wk 6) relative to best state (RBS) achieved in Anterior Chamber (AC) cell grade (Standardization of Uveitis Nomenclature [SUN] criteria)[AC cell grades range from 0 (0 cells) to 4+ (>50 cells),higher scores=severe uveitis]; Inability to achieve ≤Grade 0.5+ (at Wk 6)/2-step increase (all visits after Wk 6) RBS achieved in Vitreous Haze (VH) grade (National Eye Institute [NEI]/SUN criteria)[VH grades range from 0(no evident VH) to 4+(optic nerve head is obscured),higher scores=severe uveitis]; Worsening of best corrected visual acuity (BCVA) by ≥15 letters RBS achieved (all visits starting Wk 6),measured by an eye chart,fewer correct letters=severe uveitis. Evaluable Analysis Set.	
End point type	Primary
End point timeframe:	
Week 6 through Week (Wk) 24	

End point values	Filgotinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: percentage of participants				
number (confidence interval 95%)	37.5 (19.2 to 55.8)	67.6 (50.5 to 84.8)		

Statistical analyses

Statistical analysis title	Filgotinib vs Placebo
Comparison groups	Filgotinib v Placebo

Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0064 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Treatment Failure Rate
Point estimate	-30.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-56.2
upper limit	-4.1

Notes:

[1] - P-value was estimated from the Cochran-Mantel-Haenszel (CMH) test, adjusted for the stratification factors.

Secondary: Time to Treatment Failure on or After Week 6

End point title	Time to Treatment Failure on or After Week 6

End point description:

Treatment failure was a participant meeting at least 1 of these criteria in at least 1 eye: New active, inflammatory lesions relative to Day 1/Baseline (all visits starting Wk 6); Inability to achieve ≤Grade 0.5+ (at Wk 6) or 2-step increase (change of Grade 0 to Grade 2+/Grade 0.5+ to Grade 3+) (all visits after Wk 6) relative to best state (RBS) achieved in AC cell grade (SUN criteria) [AC cell grades range from 0 (0 cells) to 4+ (>50 cells), higher scores=severe uveitis]; Inability to achieve ≤Grade 0.5+ (at Wk 6) or 2-step increase (all visits after Wk 6) RBS achieved in VH grade (NEI/SUN criteria) [VH grades range from 0 (no evident VH) to 4+ (optic nerve head is obscured), higher scores=severe uveitis]; Worsening of BCVA by ≥15 letters RBS achieved (all visits starting Wk 6), measured by an eye chart, fewer correct letters=severe uveitis. Participants in the Evaluable Analysis Set were analyzed. 9999=Not Available as the calculated percentiles of event rate were not reached.

End point type	Secondary

End point timeframe:

Week 6 through Week 52

End point values	Filgotinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: weeks				
median (inter-quartile range (Q1-Q3))	9999 (24.1 to 9999)	22.0 (12.1 to 47.0)		

Statistical analyses

Statistical analysis title	Filgotinib vs Placebo
Comparison groups	Filgotinib v Placebo

Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0014 [2]
Method	Stratified Log-Rank Test
Parameter estimate	Stratified Hazard Ratio
Point estimate	0.309
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.144
upper limit	0.663

Notes:

[2] - P-value was derived from the log rank test stratified by the stratification factors.

Secondary: Change in Vitreous Haze (VH) Grade in Each Eye (NEI/SUN Criteria), From Best State Achieved Prior to Week 6 to Week 52 or End of Treatment (EOT) Visit or Early Termination (ET)

End point title	Change in Vitreous Haze (VH) Grade in Each Eye (NEI/SUN Criteria), From Best State Achieved Prior to Week 6 to Week 52 or End of Treatment (EOT) Visit or Early Termination (ET)

End point description:

Grading of VH was based on the publication from the NEI which has also been adapted by the SUN working group. VH grades range from 0 (no evident VH) to 4+ (optic nerve head is obscured), with higher scores indicating greater severity of uveitis. A negative change (cha) from the best value obtained prior to Week 6 indicates improvement. Participants in the Evaluable Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Prior to Week 6; Up to Week 52 or EOT or ET (maximum: 53 weeks)

End point values	Filgotinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: score				
arithmetic mean (standard deviation)				
Left Eye: Best State Prior to Wk 6 N=32,33	0.3 (± 0.40)	0.2 (± 0.33)		
Right Eye: Best State Prior to Wk 6	0.3 (± 0.36)	0.3 (± 0.45)		
Lef Eye Cha From Best State at Wk52/EOT/ET N=32,33	0.1 (± 0.79)	0.3 (± 0.75)		
Rig Eye Cha From Best State at Wk52/EOT/ET N=32,33	0.1 (± 0.62)	0.2 (± 0.66)		

Statistical analyses

Statistical analysis title	Filgotinib vs Placebo
Comparison groups	Filgotinib v Placebo

Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.355 [3]
Method	Repeated Measure ANCOVA
Parameter estimate	Least Squares Mean Treatment Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[3] - P-value was estimated using a repeated measure Analysis of Covariance (ANCOVA) model which included treatment, eye, interaction of treatment and eye, stratification factors and best state value.

Secondary: Change in Anterior Chamber (AC) Cell Grade in Each Eye, From Best State Achieved Prior to Week 6 to Week 52 or EOT Visit or ET

End point title	Change in Anterior Chamber (AC) Cell Grade in Each Eye, From Best State Achieved Prior to Week 6 to Week 52 or EOT Visit or ET

End point description:

The number of AC cells observed within a 1 mm × 1 mm slit beam were recorded for each eye. The reported number was used to determine the grade according to the SUN criteria. AC cell grades range from 0 (0 cells in field) to 4+ (>50 cells in field), with higher scores indicating more cells visible in the AC and greater severity of uveitis. A negative change from the best state value obtained prior to Week 6 indicates improvement. Participants in the Evaluable Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Prior to Week 6; Up to Week 52 or EOT or ET (maximum: 53 weeks)

End point values	Filgotinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: score				
arithmetic mean (standard deviation)				
Left Eye: Best State Prior to Wk 6	0.0 (± 0.09)	0.1 (± 0.19)		
Right Eye: Best State Prior to Wk 6	0.0 (± 0.12)	0.1 (± 0.25)		
Left Eye: Change From Best State at Wk 52/EOT/ET	0.2 (± 0.59)	0.6 (± 0.87)		
Right Eye: Change From Best State at Wk 52/EOT/ET	0.2 (± 0.53)	0.7 (± 1.05)		

Statistical analyses

Statistical analysis title	Filgotinib vs Placebo
Comparison groups	Filgotinib v Placebo

Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0145 [4]
Method	Repeated Measure ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.18

Notes:

[4] - P-value was estimated using a repeated measure ANCOVA model which included treatment, eye, interaction of treatment and eye, stratification factors and best state value.

Secondary: Change in Logarithm of the Minimal Angle of Resolution (logMAR) Best Corrected Visual Acuity (BCVA) in Each Eye, From Best State Achieved Prior to Week 6 to Week 52 or EOT Visit or ET

End point title	Change in Logarithm of the Minimal Angle of Resolution (logMAR) Best Corrected Visual Acuity (BCVA) in Each Eye, From Best State Achieved Prior to Week 6 to Week 52 or EOT Visit or ET

End point description:

BCVA is the best possible vision that an eye can achieve with the set of glasses or contact lenses. A refraction test was performed to measure the appropriate lens strength to focus light on the retina. Using the appropriate corrective lenses based on that visit's refraction, participant`s BCVA was measured using an Early Treatment Diabetic Retinopathy Study (ETDRS) chart. In the ETDRS system, 15 letters is equal to a change in 3 lines of visual acuity. If the participant is unable to read letters on a testing chart, visual acuity is described as ranging from ability to count fingers, recognize hand movements, or light perception. The smaller BVCA score indicates greater severity of uveitis. A positive change from best state value obtained prior to Week 6 indicates improvement. Participants in the Evaluable Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Prior to Week 6; Up to Week 52 or EOT or ET (maximum: 53 weeks)

End point values	Filgotinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: logMAR				
arithmetic mean (standard deviation)				
Left Eye: Best State Prior to Wk 6	0.09 (± 0.195)	0.07 (± 0.209)		
Right Eye: Best State Prior to Wk 6	0.09 (± 0.193)	0.12 (± 0.280)		
Left Eye: Change From Best State at Wk 52/EOT/ET	0.03 (± 0.154)	0.05 (± 0.112)		
Right Eye: Change From Best State at Wk 52/EOT/ET	-0.01 (± 0.116)	0.07 (± 0.144)		

Statistical analyses

Statistical analysis title	Filgotinib vs Placebo
Comparison groups	Filgotinib v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0389 [5]
Method	Repeated Measure ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.025

Notes:

[5] - P-value was estimated using a repeated measure ANCOVA model which included treatment, eye, interaction of treatment and eye, stratification factors and best state value.

Secondary: Log Change in Central Retinal Thickness in Each Eye, From Best State Achieved Prior to Week 6 to Week 52 or EOT Visit or ET

End point title	Log Change in Central Retinal Thickness in Each Eye, From Best State Achieved Prior to Week 6 to Week 52 or EOT Visit or ET

End point description:

Central retinal thickness is measured by optical coherence tomography (OCT). Central retinal thickness is defined as the thickness of the retina in the center of the foveal pit (1 mm subfield). The larger central retinal thickness value indicates greater severity of uveitis. A negative change (cha) from best state value obtained prior to Week 6 indicates improvement. Participants in the Evaluable Analysis Set with the available data were analyzed.

End point type	Secondary

End point timeframe:

Prior to Week 6; Up to Week 52 or EOT or ET (maximum: 53 weeks)

End point values	Filgotinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: log microns				
arithmetic mean (standard deviation)				
Left Eye: Best State Prior to Wk 6	2.45 (± 0.059)	2.46 (± 0.097)		
Right Eye: Best State Prior to Wk 6	2.47 (± 0.056)	2.44 (± 0.104)		

Lef Eye Cha From Best State at Wk52/EOT/ET N=32,32	0.01 (± 0.062)	0.04 (± 0.080)		
Rig Eye Cha From Best State at Wk52/EOT/ET N=32,32	0.01 (± 0.049)	0.03 (± 0.055)		

Statistical analyses

Statistical analysis title	Filgotinib vs Placebo
Comparison groups	Filgotinib v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.034 [6]
Method	Repeated Measure ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.011

Notes:

[6] - P-value was estimated using a repeated measure ANCOVA model which included treatment, eye, interaction of treatment and eye, OCT machine, and best state value.

Secondary: Time to Development of Macular Edema in At Least One Eye on or After Week 6

End point title	Time to Development of Macular Edema in At Least One Eye on or After Week 6

End point description:

Time in weeks until the development of Macular edema or Week 52 or EOT or ET. Macular edema is determined by OCT and is defined as central retinal thickness ≥ 300 microns if using Cirrus machine, or ≥ 315 microns if using Spectralis machine. Participants in the Evaluable Analysis Set were analyzed. 9999=Not Available as the calculated percentiles of event rate were not reached.

End point type	Secondary

End point timeframe:

Week 6 through Week 52

End point values	Filgotinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: weeks				
median (inter-quartile range (Q1-Q3))	7.8 (6.1 to 9999)	12.3 (6.1 to 9999)		

Statistical analyses

Statistical analysis title	Filgotinib vs Placebo
Comparison groups	Filgotinib v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5893 [7]
Method	Stratified Log-Rank Test
Parameter estimate	Stratified Hazard Ratio
Point estimate	1.193
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.625
upper limit	2.277

Notes:

[7] - P-value was derived from the log rank test stratified by the stratification factors.

Secondary: Plasma Concentration of Filgotinib

End point title	Plasma Concentration of Filgotinib[8]

End point description:

Participants in the Safety Analysis Set who have at least one non-missing concentration data with available data were analyzed.

End point type	Secondary

End point timeframe:

Day 1 post dose, Weeks 4 and 6 predose, Week 12 post dose, Weeks 24, 36, 52 (EOT), Early Termination at any time

Notes:

[8] - 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: Plasma concentrations were collected and analyzed for filgotinib arm group.

End point values	Filgotinib			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: nanograms per millilitre (ng/ml)				
arithmetic mean (standard deviation)				
Day 1 Postdose	748.5 (± 1043.84)			
Week 4 Predose (N=29)	173.3 (± 364.46)			
Week 6 Predose (N=28)	133.9 (± 306.18)			
Week 12 Postdose (N=27)	1088.7 (± 856.57)			

Week 24 Single Anytime (N=21)	397.5 (± 561.57)			
Week 36 Single Anytime (N=14)	295.7 (± 420.25)			
Week 52 (EOT) Single Anytime (N=22)	195.2 (± 344.54)			
Early Termination Single Anytime (N=3)	434.8 (± 478.72)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Metabolite, GS-829845

End point title	Plasma Concentration of Metabolite, GS-829845[9]

End point description:

Participants in the Safety Analysis Set who have at least one non-missing concentration data with available data were analyzed.

End point type	Secondary

End point timeframe:

Day 1 post dose, Weeks 4 and 6 predose, Week 12 post dose, Weeks 24, 36, 52 (EOT), Early Termination at any time

Notes:

[9] - 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: Plasma concentrations were collected and analyzed for filgotinib arm group.

End point values	Filgotinib			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: ng/ml				
arithmetic mean (standard deviation)				
Day 1 Postdose	230.8 (± 317.98)			
Week 4 Predose (N=29)	2085.6 (± 924.91)			
Week 6 Predose (N=28)	2107.7 (± 749.28)			
Week 12 Postdose (N=27)	3237.0 (± 1180.74)			
Week 24 Single Anytime (N=21)	3478.1 (± 1137.63)			
Week 36 Single Anytime (N=14)	2944.3 (± 1130.84)			
Week 52 (EOT) Single Anytime (N=22)	2510.7 (± 1732.59)			
Early Termination Single Anytime (N=3)	2171.0 (± 1224.77)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: First dose date up to 30 days after the last dose of study drug (maximum exposure up to 57 weeks); All-Cause Mortality: From randomization up to 57 weeks

Adverse event reporting additional description:

Adverse Events: Safety Analysis Set included all participants who received at least 1 dose of study drug. All- Cause Mortality: All Randomized Analysis Set included all participants who were randomized in the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Filgotinib

Reporting group description:

Participants received filgotinib 200 mg tablet orally, once daily for up to 52 weeks along with a standardized prednisone burst of 60 mg/day at Day 1/Baseline followed by a protocol-defined mandatory taper schedule up to Week 15.

Reporting group title	Placebo

Reporting group description:

Participants received placebo to match filgotinib tablet orally, once daily for up to 52 weeks along with a standardized prednisone burst of 60 mg/day at Day 1/Baseline followed by a protocol-defined mandatory taper schedule up to Week 15.

Serious adverse events	Filgotinib	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 37 (13.51%)	2 / 35 (5.71%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 37 (2.70%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal vasculitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uveitis			

subjects affected / exposed	1 / 37 (2.70%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Inflammatory bowel disease			
subjects affected / exposed	1 / 37 (2.70%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	1 / 37 (2.70%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Bladder prolapse			
subjects affected / exposed	1 / 37 (2.70%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Spinal stenosis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Covid-19			
subjects affected / exposed	1 / 37 (2.70%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Filgotinib	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 37 (75.68%)	19 / 35 (54.29%)	
Investigations			
Intraocular pressure increased			
subjects affected / exposed	2 / 37 (5.41%)	2 / 35 (5.71%)	
occurrences (all)	2	2	
Weight increased			
subjects affected / exposed	3 / 37 (8.11%)	1 / 35 (2.86%)	
occurrences (all)	3	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	3 / 37 (8.11%)	0 / 35 (0.00%)	
occurrences (all)	3	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 37 (2.70%)	3 / 35 (8.57%)	
occurrences (all)	2	3	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 37 (8.11%)	7 / 35 (20.00%)	
occurrences (all)	4	7	
Dizziness			
subjects affected / exposed	3 / 37 (8.11%)	0 / 35 (0.00%)	
occurrences (all)	3	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 37 (8.11%)	3 / 35 (8.57%)	
occurrences (all)	3	3	
Eye disorders			
Dry eye			
subjects affected / exposed	2 / 37 (5.41%)	4 / 35 (11.43%)	
occurrences (all)	2	4	
Visual impairment			
subjects affected / exposed	5 / 37 (13.51%)	1 / 35 (2.86%)	
occurrences (all)	5	1	

Chorioretinal disorder			
subjects affected / exposed	2 / 37 (5.41%)	2 / 35 (5.71%)	
occurrences (all)	2	2	
Eye irritation			
subjects affected / exposed	2 / 37 (5.41%)	2 / 35 (5.71%)	
occurrences (all)	2	2	
Uveitis			
subjects affected / exposed	2 / 37 (5.41%)	2 / 35 (5.71%)	
occurrences (all)	2	2	
Vitreous floaters			
subjects affected / exposed	3 / 37 (8.11%)	1 / 35 (2.86%)	
occurrences (all)	3	1	
Anterior chamber inflammation			
subjects affected / exposed	1 / 37 (2.70%)	2 / 35 (5.71%)	
occurrences (all)	1	2	
Cataract			
subjects affected / exposed	2 / 37 (5.41%)	1 / 35 (2.86%)	
occurrences (all)	2	1	
Eye pain			
subjects affected / exposed	2 / 37 (5.41%)	1 / 35 (2.86%)	
occurrences (all)	2	1	
Macular oedema			
subjects affected / exposed	2 / 37 (5.41%)	1 / 35 (2.86%)	
occurrences (all)	2	1	
Photopsia			
subjects affected / exposed	3 / 37 (8.11%)	0 / 35 (0.00%)	
occurrences (all)	3	0	
Chalazion			
subjects affected / exposed	0 / 37 (0.00%)	2 / 35 (5.71%)	
occurrences (all)	0	2	
Ocular hyperaemia			
subjects affected / exposed	2 / 37 (5.41%)	0 / 35 (0.00%)	
occurrences (all)	2	0	
Photophobia			
subjects affected / exposed	2 / 37 (5.41%)	0 / 35 (0.00%)	
occurrences (all)	2	0	

Vitreous haze			
subjects affected / exposed	2 / 37 (5.41%)	0 / 35 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 37 (10.81%)	1 / 35 (2.86%)	
occurrences (all)	4	1	
Abdominal pain			
subjects affected / exposed	4 / 37 (10.81%)	0 / 35 (0.00%)	
occurrences (all)	4	0	
Diarrhoea			
subjects affected / exposed	2 / 37 (5.41%)	2 / 35 (5.71%)	
occurrences (all)	2	2	
Dyspepsia			
subjects affected / exposed	3 / 37 (8.11%)	1 / 35 (2.86%)	
occurrences (all)	3	1	
Abdominal distension			
subjects affected / exposed	2 / 37 (5.41%)	0 / 35 (0.00%)	
occurrences (all)	2	0	
Constipation			
subjects affected / exposed	2 / 37 (5.41%)	0 / 35 (0.00%)	
occurrences (all)	2	0	
Dry mouth			
subjects affected / exposed	2 / 37 (5.41%)	0 / 35 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Upper-airway cough syndrome			
subjects affected / exposed	2 / 37 (5.41%)	2 / 35 (5.71%)	
occurrences (all)	2	2	
Sleep apnoea syndrome			
subjects affected / exposed	2 / 37 (5.41%)	0 / 35 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 37 (10.81%)	4 / 35 (11.43%)	
occurrences (all)	4	4	

Anxiety			
subjects affected / exposed	2 / 37 (5.41%)	2 / 35 (5.71%)	
occurrences (all)	2	2	
Depression			
subjects affected / exposed	2 / 37 (5.41%)	1 / 35 (2.86%)	
occurrences (all)	2	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 37 (8.11%)	2 / 35 (5.71%)	
occurrences (all)	4	2	
Back pain			
subjects affected / exposed	3 / 37 (8.11%)	1 / 35 (2.86%)	
occurrences (all)	3	1	
Pain in extremity			
subjects affected / exposed	2 / 37 (5.41%)	2 / 35 (5.71%)	
occurrences (all)	2	2	
Myalgia			
subjects affected / exposed	1 / 37 (2.70%)	2 / 35 (5.71%)	
occurrences (all)	1	2	
Muscle spasms			
subjects affected / exposed	2 / 37 (5.41%)	0 / 35 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 37 (0.00%)	2 / 35 (5.71%)	
occurrences (all)	0	2	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	4 / 37 (10.81%)	3 / 35 (8.57%)	
occurrences (all)	6	3	
Upper respiratory tract infection			
subjects affected / exposed	3 / 37 (8.11%)	2 / 35 (5.71%)	
occurrences (all)	3	3	
Bronchitis			
subjects affected / exposed	1 / 37 (2.70%)	2 / 35 (5.71%)	
occurrences (all)	1	2	
Covid-19			

subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	0 / 35 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 November 2017	• ECG collection at the Screening visit only. • Allowed for the safety laboratory assessments to be performed locally or centrally at Screening visit only. • Removed lens photography and reduced fundus photography assessments. • Removed sarcoidosis assessments and sarcoidosis imaging requirements. • Clarified requirements for Unscheduled visits related to uveitis symptoms. • Updated Inclusion criteria to clarify oral corticosteroid requirements prior to Day 1 dosing. • Updated Exclusion criteria to clarify severe glaucoma. • Updated Inclusion criteria to clarify QuantiFERON® TB Gold and TB testing requirements. • Updated Exclusion criteria to clarify immunosuppressive therapy. • Updated Exclusion criteria to clarify concomitant immunosuppressive therapy. • Updated Exclusion criteria to exclude eyelid surgery from prior ocular surgery. • Updated Exclusion criteria to exclude eyelid surgery from planned (elective) eye surgery. • Updated Exclusion criteria to clarify HIV and Syphilis testing requirements. • Updated Exclusion criteria to define marijuana and tobacco use. • Updated storage and handling conditions for filgotinib. • Updated tonometry requirements. • Updated Fluorescein Angiogram requirements. • Updated risk/benefit assessment language. • Updated study drug return or disposal language. • Updated study schema. • Updated prohibited medications. • Updated study title. • Updated pregnancy precautions, definition for female of childbearing potential, and contraceptive requirements. • Updated clinical laboratory assessment table. • Updated references. • Added Ct.gov NCT number.
18 December 2017	• Updated synopsis, study design to correct inconsistencies made when incorporating changes into protocol amendment 1. • Updated synopsis and main eligibility criteria to correct inconsistencies between changes outlined in the summary of changes document and protocol amendment 1. • Updated synopsis, study procedures/frequency to delete lipid profile from screening. • Updated Inclusion criteria to correct inconsistencies made when incorporating changes into protocol amendment 1. • Updated subscripts to provide clarity around HBV Viral Monitoring and also, childbearing potential. • Updated to clarify the definition of childbearing potential.
12 December 2019	• Relaxation of entry criteria to allow participants that have previously failed anti-TNF treatment. • Relaxation of entry criteria to allow participants with previously treated active or latent TB. • DSPH (Drug Safety and Public Health) was replaced by PVE (Pharmacovigilance & Epidemiology) within the whole document.

17 March 2020	• Expand the sample size to N = 248 participants. • Expand the number of sites globally to approximately 75 centers. • Incorporate an independent adjudication committee to review major adverse cardiovascular events and thromboembolic events. • Add a new study drug discontinuation criterion: any thromboembolic events meeting serious adverse event (SAE) reporting criteria. • Language regarding independent adjudication committee reviews for major adverse cardiovascular events and thromboembolic events has been updated throughout the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
20 March 2020	There were global interruptions to enrollment due to corona virus disease 2019 (COVID-19) outbreak, measures were taken to introduce a global screening halt. Decision to restart enrolment was made on data monitoring committee (DMC) recommendation.	21 May 2020

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Study was terminated early due to termination of the development program. Due to early termination and small sample size, PK analysis was not performed for this study.

Notes: