Clinical trial results:
A Phase 2, Double-Blind, Randomized, Placebo-Controlled Study Evaluating the Efficacy and Safety of Filgotinib in the Treatment of Small Bowel Crohn's Disease (SBCD)

Summary

EudraCT number	2016-003179-23
Trial protocol	GB DE CZ ES PL HU FR AT BE IT
Global end of trial date	20 July 2020

Results information

Result version number	v1
This version publication date	04 August 2021
First version publication date	04 August 2021

Trial information

Trial identification

Sponsor protocol code	GS-US-419-4015

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03046056
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 July 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 July 2020
Global end of trial reached?	Yes
Global end of trial date	20 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy of filgotinib, when compared to placebo, in establishing clinical remission defined as crohn's disease activity index (CDAI) < 150, at Week 24 in participants with crohn's disease (CD) involving the small bowel. Participants had the option to enter a separate long-term extension study if they met the eligibility requirements.

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	11 April 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	United States: 38
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Ukraine: 3
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Czechia: 1
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	Italy: 5
Worldwide total number of subjects	78
EEA total number of subjects	25

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)	71
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States, Canada, and Europe. The first participant was screened on 11 April 2017. The last study visit occurred on 20 July 2020.

Pre-assignment

Screening details:

177 participants were screened.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Filgotinib 200 mg

Arm description:

Filgotinib 200 mg tablet + placebo to match (PTM) filgotinib 100 mg tablet orally once daily for up to 27 weeks.

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

Dosage and administration details:

200 mg tablet administered once daily

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

Dosage and administration details:

PTM filgotinib 100 mg administered once daily

Arm title	Filgotinib 100 mg

Arm description:

Filgotinib 100 mg tablet + PTM filgotinib 200 mg tablet orally once daily for up to 26.3 weeks.

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

Dosage and administration details:

100 mg tablet administered once daily

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

Dosage and administration details:
PTM filgotinib 200 mg administered once daily

Arm title	Placebo

Arm description:
PTM filgotinib 200 mg tablet + PTM filgotinib 100 mg tablet orally once daily for up to 28.7 weeks.

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

Dosage and administration details:
PTM filgotinib 100 mg administered once daily

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

Dosage and administration details:
PTM filgotinib 200 mg administered once daily

Number of subjects in period 1	Filgotinib 200 mg	Filgotinib 100 mg	Placebo
Started	28	32	18
Completed	16	16	11
Not completed	12	16	7
Withdrew Consent	1	-	-
Protocol-specified disease worsening	3	3	1
Adverse Event	1	5	-
Non-compliance with study drug	-	-	2
Protocol Violation	1	1	-
Non-responder at Week 10	6	6	4
Investigator's discretion	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Filgotinib 200 mg
Reporting group description:	
Filgotinib 200 mg tablet + placebo to match (PTM) filgotinib 100 mg tablet orally once daily for up to 27 weeks.	
Reporting group title	Filgotinib 100 mg
Reporting group description:	
Filgotinib 100 mg tablet + PTM filgotinib 200 mg tablet orally once daily for up to 26.3 weeks.	
Reporting group title	Placebo
Reporting group description:	
PTM filgotinib 200 mg tablet + PTM filgotinib 100 mg tablet orally once daily for up to 28.7 weeks.	

Reporting group values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo
Number of subjects	28	32	18
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	46	42	45
standard deviation	± 16.3	± 12.9	± 12.9
Gender categorical Units: Subjects			
Female	19	23	9
Male	9	9	9
Race			
Not Permitted means local regulators did not allow collection of race information.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Black or African American	2	4	2
Native Hawaiian or Pacific Islander	0	0	0
White	25	28	16
Other	1	0	0
Not Permitted	0	0	0
Ethnicity			
Not Permitted means local regulators did not allow collection of ethnicity information.			
Units: Subjects			
Not Hispanic or Latino	26	31	17
Hispanic or Latino	2	1	1
Not Permitted	0	0	0
Crohn’s Disease Activity Index Score (CDAI)			
The CDAI score is used to quantify the symptoms of participants with Crohn's Disease. The score ranges from 0 to 600. A score of < 150 indicates remission. A higher score indicates more severe disease.			
Units: score on scale			

arithmetic mean	309	297	300
standard deviation	± 55.7	± 64.9	± 63.7

Reporting group values	Total		
Number of subjects	78		
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	51		
Male	27		
Race			
Not Permitted means local regulators did not allow collection of race information.			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Black or African American	8		
Native Hawaiian or Pacific Islander	0		
White	69		
Other	1		
Not Permitted	0		
Ethnicity			
Not Permitted means local regulators did not allow collection of ethnicity information.			
Units: Subjects			
Not Hispanic or Latino	74		
Hispanic or Latino	4		
Not Permitted	0		
Crohn’s Disease Activity Index Score (CDAI)			
The CDAI score is used to quantify the symptoms of participants with Crohn's Disease. The score ranges from 0 to 600. A score of < 150 indicates remission. A higher score indicates more severe disease.			
Units: score on scale arithmetic mean standard deviation	 -		

End points

End points reporting groups	
Reporting group title	Filgotinib 200 mg
Reporting group description:	
Filgotinib 200 mg tablet + placebo to match (PTM) filgotinib 100 mg tablet orally once daily for up to 27 weeks.	
Reporting group title	Filgotinib 100 mg
Reporting group description:	
Filgotinib 100 mg tablet + PTM filgotinib 200 mg tablet orally once daily for up to 26.3 weeks.	
Reporting group title	Placebo
Reporting group description:	
PTM filgotinib 200 mg tablet + PTM filgotinib 100 mg tablet orally once daily for up to 28.7 weeks.	

Primary: Percentage of Participants Who Achieved Clinical Remission at Week 24	
End point title	Percentage of Participants Who Achieved Clinical Remission at Week 24
End point description:	
The CDAI score is used to quantify the symptoms of participants with Crohn's Disease (CD). The score ranges from 0 to 600. Clinical remission by CDAI was defined as a score of < 150. A higher score indicates more severe disease. Full Analysis Set included all the randomized participants who received at least one dose of the study drug.	
End point type	Primary
End point timeframe:	
Week 24	

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	32	18	
Units: percentage of participants				
number (confidence interval 90%)	25.0 (12.4 to 41.9)	25.0 (13.1 to 40.6)	16.7 (4.7 to 37.7)	

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo
Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	8.3

Confidence interval	
level	90 %
sides	2-sided
lower limit	-16.5
upper limit	32.1

Statistical analysis title	Filgotinib 100 mg vs Placebo
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	8.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-15.9
upper limit	32

Secondary: Change From Baseline in Terminal Ileum Segmental Magnetic Resonance Index of Activity (MaRIA) Score at Week 24

End point title	Change From Baseline in Terminal Ileum Segmental Magnetic Resonance Index of Activity (MaRIA) Score at Week 24

End point description:

Magnetic resonance enterography (MRE) is an imaging technique to evaluate disease activity in CD. MaRIA is an MRE-based scoring system, a composite index of 4 components. They are edema, ulcers, gut wall thickness, and relative contrast enhancement (RCE). A segmental MaRIA score is calculated at screening (used as the baseline) and Week 24 for each of the 3 small bowel segments (terminal ileum, jejunum, and duodenum). A segmental score of ≥ 7 indicates active inflammation and a score of ≥ 11 indicates the presence of an ulcer. Segmental scores less than 7 indicates remission. The MaRIA score ranges from approximately 0 to 31, for any given segment. A higher score indicates more severe disease. Difference in least squared means (Diff in LSM) were from analysis of covariance (ANCOVA) model. A negative change from baseline indicates improvement and a positive change from baseline indicates disease worsening. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	32	18	
Units: score				
least squares mean (standard error)	-1.8 (± 1.51)	0.7 (± 1.39)	0.5 (± 1.64)	

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo

Statistical analysis description:

Difference in least squared means (Diff in LSM), and its 90% CI were from analysis of covariance (ANCOVA) model adjusted by baseline segmental MaRIA score, concomitant use of oral, systemically absorbed corticosteroids at baseline, concomitant use of immunomodulators at baseline, prior exposure to biologics, and treatment group.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least Squares Mean Difference
Point estimate	-2.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.3
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	1.81

Statistical analysis title	Filgotinib 100 mg vs Placebo

Statistical analysis description:

Diff in LSM, and its 90% CI were from ANCOVA model adjusted by baseline segmental MaRIA score, concomitant use of oral, systemically absorbed corticosteroids at baseline, concomitant use of immunomodulators at baseline, prior exposure to biologics, and treatment group.

Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least Squares Mean Difference
Point estimate	0.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.7
upper limit	3.1
Variability estimate	Standard error of the mean
Dispersion value	1.72

Secondary: Change From Baseline in Distal Ileum Segmental MaRIA Score at Week 24

End point title	Change From Baseline in Distal Ileum Segmental MaRIA Score at Week 24

End point description:

MRE is an imaging technique to evaluate disease activity in CD. MaRIA is an MRE-based scoring system. The MaRIA scoring system is a composite index of 4 components. These components are edema, ulcers, gut wall thickness, and RCE. A segmental MaRIA score can be calculated at Screening (used as the baseline) and Week 24 as a weighted sum of these 4 components for each of the 3 small bowel segments (terminal ileum, jejunum, and duodenum).A segmental score of ≥ 7 indicates active inflammation and a score of ≥ 11 indicates the presence of an ulcer. Segmental scores less than 7 indicate remission in that segment. The MaRIA score ranges from approximately 0 to 31, for any given segment. A higher score indicates more severe disease. Diff in LSM were from ANCOVA model. A negative change from baseline indicates improvement and a positive change from baseline indicates disease worsening. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	32	18	
Units: score				
least squares mean (standard error)	-1.1 (± 1.12)	-0.5 (± 1.08)	0.5 (± 1.26)	

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo

Statistical analysis description:

Diff in LSM, and its 90% CI were from ANCOVA model adjusted by baseline segmental MaRIA score, concomitant use of oral, systemically absorbed corticosteroids at baseline, concomitant use of immunomodulators at baseline, prior exposure to biologics, and treatment group.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least Squares Mean Difference
Point estimate	-1.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.9
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	1.38

Statistical analysis title	Filgotinib 100 mg vs Placebo

Statistical analysis description:

Diff in LSM, and its 90% CI were from ANCOVA model adjusted by baseline segmental MaRIA score, concomitant use of oral, systemically absorbed corticosteroids at baseline, concomitant use of immunomodulators at baseline, prior exposure to biologics, and treatment group.

Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least Squares Mean Difference
Point estimate	-1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.2
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	1.32

Secondary: Change From Baseline in Jejunum Segmental MaRIA Score at Week 24

End point title	Change From Baseline in Jejunum Segmental MaRIA Score at Week 24

End point description:

MRE is an imaging technique to evaluate disease activity in CD. MaRIA is an MRE-based scoring system.The MaRIA scoring system is a composite index of 4 components. These components are edema, ulcers, gut wall thickness, and RCE. A segmental MaRIA score can be calculated at Screening (used as the baseline) and Week 24 as a weighted sum of these 4 components for each of the 3 small bowel segments (terminal ileum, jejunum, and duodenum). A segmental score of ≥ 7 indicates active inflammation and a score of ≥ 11 indicates the presence of an ulcer. Segmental scores less than 7 indicate remission in that segment. The MaRIA score ranges from approximately 0 to 31, for any given segment. A higher score indicates more severe disease. Diff in LSM were from ANCOVA model. A positive change from baseline indicates disease worsening. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	32	18	
Units: score				
least squares mean (standard error)	0.4 (± 1.00)	0.6 (± 0.95)	0.5 (± 1.12)	

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo

Statistical analysis description:

Diff in LSM, and its 90% CI were from ANCOVA model adjusted by baseline segmental MaRIA score, concomitant use of oral, systemically absorbed corticosteroids at baseline, concomitant use of immunomodulators at baseline, prior exposure to biologics, and treatment group.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least Squares Mean Difference
Point estimate	-0.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.2
upper limit	2
Variability estimate	Standard error of the mean
Dispersion value	1.24

Statistical analysis title	Filgotinib 100 mg vs Placebo

Statistical analysis description:

Diff in LSM, and its 90% CI were from ANCOVA model adjusted by baseline segmental MaRIA score, concomitant use of oral, systemically absorbed corticosteroids at baseline, concomitant use of immunomodulators at baseline, prior exposure to biologics, and treatment group.

Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least Squares Mean Difference
Point estimate	0.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.9
upper limit	2
Variability estimate	Standard error of the mean
Dispersion value	1.18

Secondary: Percentage of Participants who Achieved MaRIA Remission in Terminal Ileum Segment at Week 24

End point title	Percentage of Participants who Achieved MaRIA Remission in Terminal Ileum Segment at Week 24

End point description:

The MaRIA scoring system is a composite index of 4 components. These components are edema, ulcers, gut wall thickness, and RCE. A segmental MaRIA score can be calculated at screening (used as the baseline) and Week 24 as a weighted sum of these 4 components for each of the 3 small bowel segments. The MaRIA score ranges from approximately 0 to 31, for any given segment. A higher score indicates more severe disease. MaRIA remission was defined as a segmental MaRIA score < 7 in terminal ileum segment at Week 24 among participants with MaRIA score ≥ 7 in the same segment at

baseline. A segmental score of ≥ 7 indicates active inflammation and a score of ≥ 11 indicates the presence of an ulcer. Participants in the Full Analysis Set with active disease (segmental MaRIA score ≥ 7) in terminal ileum segment at baseline, were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	30	16	
Units: percentage of participants				
number (confidence interval 90%)	4.5 (0.2 to 19.8)	6.7 (1.2 to 19.5)	6.3 (0.3 to 26.4)	

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo
Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	-1.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-28.6
upper limit	25.5

Statistical analysis title	Filgotinib 100 mg vs Placebo
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	0.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-24.5
upper limit	26.2

Secondary: Percentage of Participants Who Achieved MaRIA Remission in Distal Ileum Segment at Week 24

End point title	Percentage of Participants Who Achieved MaRIA Remission in Distal Ileum Segment at Week 24

End point description:

The MaRIA scoring system is a composite index of 4 components. These components are edema, ulcers, gut wall thickness, and RCE. A segmental MaRIA score can be calculated at screening (used as the baseline) and Week 24 as a weighted sum of these 4 components for each of the 3 small bowel segments. The MaRIA score ranges from approximately 0 to 31, for any given segment. A higher score indicates more severe disease. MaRIA remission was defined as a segmental MaRIA score < 7 in distal ileum segment at Week 24 among participants with MaRIA score ≥ 7 in the same segment at baseline. A segmental score of ≥ 7 indicates active inflammation and a score of ≥ 11 indicates the presence of an ulcer. Participants in the Full Analysis Set with active disease (segmental MaRIA score ≥ 7) in distal ileum segment at baseline, were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	6	
Units: percentage of participants				
number (confidence interval 90%)	10.0 (0.5 to 39.4)	0 (0.0 to 31.2)	16.7 (0.9 to 58.2)	

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo
Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	-6.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-47.3
upper limit	37

Statistical analysis title	Filgotinib 100 mg vs Placebo
Comparison groups	Filgotinib 100 mg v Placebo

Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	-16.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-58.2
upper limit	30

Secondary: Percentage of Participants Who Achieved MaRIA Remission in Jejunum Segment at Week 24

End point title	Percentage of Participants Who Achieved MaRIA Remission in Jejunum Segment at Week 24

End point description:

The MaRIA scoring system is a composite index of 4 components. These components are edema, ulcers, gut wall thickness, and RCE. A segmental MaRIA score can be calculated at screening (used as the baseline) and Week 24 as a weighted sum of these 4 components for each of the 3 small bowel segments. The MaRIA score ranges from approximately 0 to 31, for any given segment. A higher score indicates more severe disease. MaRIA remission was defined as a segmental MaRIA score < 7 in jejunum segment at Week 24 among participants with MaRIA score ≥ 7 in the same segment at baseline. A segmental score of ≥ 7 indicates active inflammation and a score of ≥ 11 indicates the presence of an ulcer. Participants in the Full Analysis Set with active disease (segmental MaRIA score ≥ 7) in jejunum segment at baseline, were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	8	3	
Units: percentage of participants				
number (confidence interval 90%)	33.3 (6.3 to 72.9)	0 (0.0 to 31.2)	0 (0.0 to 63.2)	

Statistical analyses

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

Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	33.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-32.4
upper limit	86.5

Secondary: Percentage of Participants Who Achieved MaRIA Response in Terminal Ileum Segment at Week 24

End point title	Percentage of Participants Who Achieved MaRIA Response in Terminal Ileum Segment at Week 24

End point description:

The MaRIA scoring system is a composite index of 4 components. These components are edema, ulcers, gut wall thickness, and RCE. A segmental MaRIA score can be calculated at screening (used as the baseline) and Week 24 as a weighted sum of these 4 components for each of the 3 small bowel segment. The MaRIA score ranges from approximately 0 to 31, for any given segment. A higher score indicates more severe disease. MaRIA response was defined as a segmental MaRIA score < 11 with baseline score ≥ 11, or a segmental MaRIA score < 7 with baseline score ≥ 7, or ≥ minimum detectable difference (MDD) units decrease from baseline score for segments with baseline MaRIA score ≥ 7 in the terminal ileum. For segments with baseline MaRIA score ≥ 15, the MDD is 6.5 units and for baseline MaRIA score < 15, the MDD is 4.0 units. Participants in the Full Analysis Set with active disease (segmental MaRIA score ≥ 7) in terminal ileum segment at baseline, were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	30	16	
Units: percentage of participants				
number (confidence interval 90%)	22.7 (9.4 to 42.0)	10.0 (2.8 to 23.9)	25.0 (9.0 to 48.4)	

Statistical analyses

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

Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	-2.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-28.6
upper limit	24.3

Statistical analysis title	Filgotinib 100 mg vs Placebo
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	-15
Confidence interval	
level	90 %
sides	2-sided
lower limit	-39.4
upper limit	11.3

Secondary: Percentage of Participants Who Achieved MaRIA Response in Distal Ileum Segment at Week 24

End point title	Percentage of Participants Who Achieved MaRIA Response in Distal Ileum Segment at Week 24

End point description:

The MaRIA scoring system is a composite index of 4 components. These components are edema, ulcers, gut wall thickness, and RCE. A segmental MaRIA score can be calculated at screening (used as the baseline) and Week 24 as a weighted sum of these 4 components for each of the 3 small bowel segments. The MaRIA score ranges from approximately 0 to 31, for any given segment. A higher score indicates more severe disease. MaRIA response was defined as a segmental MaRIA score < 11 with baseline score ≥ 11, or a segmental MaRIA score < 7 with baseline score ≥ 7, or ≥ MDD units decrease from baseline score for segments with baseline MaRIA score≥ 7 in the distal ileum. For segments with baseline MaRIA score ≥ 15, the minimum detectable difference (MDD) is 6.5 units and for baseline MaRIA score < 15, the MDD is 4.0 units. Participants in the Full Analysis Set with active disease (segmental MaRIA score ≥ 7) in distal ileum segment at baseline, were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	6	
Units: percentage of participants				
number (confidence interval 90%)	20.0 (3.7 to 50.7)	12.5 (0.6 to 47.1)	16.7 (0.9 to 58.2)	

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo
Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	3.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-38.9
upper limit	45.7

Statistical analysis title	Filgotinib 100 mg vs Placebo
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	-4.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-47.5
upper limit	40.8

Secondary: Percentage of Participants Who Achieved MaRIA Response in Jejunum Segment at Week 24

End point title	Percentage of Participants Who Achieved MaRIA Response in Jejunum Segment at Week 24

End point description:

The MaRIA scoring system is a composite index of 4 components. These components are edema, ulcers, gut wall thickness, and RCE. A MaRIA score can be calculated at screening and Week 24 for each of the 3 small bowel segments. The MaRIA score ranges from approximately 0 to 31, for any given segment. A higher score indicates more severe disease. MaRIA response was defined as a segmental MaRIA score < 11 with baseline score ≥ 11, or a segmental MaRIA score < 7 with baseline score ≥ 7, or ≥ MDD units decrease from baseline score for segments with baseline MaRIA score ≥ 7 in the jejunum. A segmental

score of ≥ 7 indicates active inflammation and a score of ≥ 11 indicates the presence of an ulcer. For segments with baseline MaRIA score ≥ 15, the MDD is 6.5 units and for baseline MaRIA score < 15, the MDD is 4.0 units. Participants in the Full Analysis Set with active disease (segmental MaRIA score ≥ 7) in jejunum segment at baseline, were analyzed.

End point type	Secondary
End point timeframe:	
Week 24	

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	8	3	
Units: percentage of participants				
number (confidence interval 90%)	50.0 (15.3 to 84.7)	12.5 (0.6 to 47.1)	0 (0.0 to 63.2)	

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo
Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	50
Confidence interval	
level	90 %
sides	2-sided
lower limit	-16.8
upper limit	89.5

Statistical analysis title	Filgotinib 100 mg vs Placebo
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	12.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-46.1
upper limit	63.3

Secondary: Percentage of Participants Who Achieved Participant Level Small Bowel MaRIA Remission at Week 24

End point title	Percentage of Participants Who Achieved Participant Level Small Bowel MaRIA Remission at Week 24

End point description:

The MaRIA scoring system is a composite index of 4 components. These components are edema, ulcers, gut wall thickness, and RCE. A segmental MaRIA score can be calculated at screening (used as the baseline) and Week 24 as a weighted sum of these 4 components for each of the 3 small bowel segments. The MaRIA score ranges from approximately 0 to 31, for any given segment. A higher score indicates more severe disease. Small bowel MaRIA remission was defined as MaRIA score < 7 at Week 24 in each of the 3 small bowel segments, among participants with MaRIA score ≥ 7 in at least 1 small bowel segment at baseline. Participants in the Full Analysis Set with active disease (segmental MaRIA score ≥ 7) in at least 1 small bowel segment at baseline, were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	32	18	
Units: percentage of participants				
number (confidence interval 90%)	8.0 (1.4 to 23.1)	6.3 (1.1 to 18.4)	0 (0.0 to 15.3)	

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo
Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-17.2
upper limit	32.6

Statistical analysis title	Filgotinib 100 mg vs Placebo
Comparison groups	Filgotinib 100 mg v Placebo

Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	6.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-18.1
upper limit	30.2

Secondary: Percentage of Participants Who Achieved Participant Level Small Bowel MaRIA Response at Week 24

End point title	Percentage of Participants Who Achieved Participant Level Small Bowel MaRIA Response at Week 24

End point description:

The MaRIA scoring system is a composite index of 4 components. These components are edema, ulcers, gut wall thickness, and RCE. A segmental MaRIA score can be calculated at screening (used as the baseline) and Week 24 as a weighted sum of these 4 components for each of the 3 small bowel segments. The MaRIA score ranges from approximately 0 to 31, for any given segment. A higher score indicates more severe disease. Participant level small bowel MaRIA response was defined as all small bowel segments with baseline MaRIA score ≥7 achieve segment level MaRIA response, with no segment level disease worsening in any other segment(s) at Week 24, among participants with MaRIA score ≥ 7 in at least 1 small bowel segment at baseline. Participants in the Full Analysis Set with active disease (segmental MaRIA score ≥ 7) in at least 1 small bowel segment at baseline, were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	32	18	
Units: percentage of participants				
number (confidence interval 90%)	20.0 (8.2 to 37.5)	12.5 (4.4 to 26.4)	16.7 (4.7 to 37.7)	

Statistical analyses

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

Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	3.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-22.1
upper limit	28.1

Statistical analysis title	Filgotinib 100 mg vs Placebo
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	-4.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-28.1
upper limit	20.3

Secondary: Percentage of Participants who Achieved Early Clinical Remission by Crohn's Disease Activity Index (CDAI) at Week 10

End point title	Percentage of Participants who Achieved Early Clinical Remission by Crohn's Disease Activity Index (CDAI) at Week 10

End point description:

The CDAI score is used to quantify the symptoms of participants with CD. The score ranges from 0 to 600. Clinical remission by CDAI was defined as a score of < 150. A higher score indicates more severe disease. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Week 10

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	32	18	
Units: percentage of participants				
number (confidence interval 90%)	39.3 (23.8 to 56.5)	25.0 (13.1 to 40.6)	22.2 (8.0 to 43.9)	

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo
Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	17.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.6
upper limit	40.4

Statistical analysis title	Filgotinib 100 mg vs Placebo
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	2.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-21.2
upper limit	26.5

Secondary: Change From Baseline in CDAI Scores at Week 10	
End point title	Change From Baseline in CDAI Scores at Week 10
End point description:	
The CDAI score is used to quantify the symptoms of participants with CD. The score ranges from 0 to 600. A score of < 150 indicates remission. A higher score indicates more severe disease. Difference in least squared means (Diff in LSM) were from analysis of covariance (ANCOVA) model. A negative change from baseline indicates improvement. Participants in the Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline; Week 10	

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	32	18	
Units: score on scale				
least squares mean (standard error)	-105 (± 23.6)	-88 (± 22.3)	-57 (± 26.2)	

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo
Statistical analysis description:	
Diff in LSM, and its 90% CI were from ANCOVA model adjusted by baseline segmental MaRIA score, concomitant use of oral, systemically absorbed corticosteroids at baseline, concomitant use of immunomodulators at baseline, prior exposure to biologics, and treatment group.	
Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least Squares Mean Difference
Point estimate	-48
Confidence interval	
level	90 %
sides	2-sided
lower limit	-95
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	28.1

Statistical analysis title	Filgotinib 100 mg vs Placebo
Statistical analysis description:	
Diff in LSM, and its 90% CI were from ANCOVA model adjusted by baseline segmental MaRIA score, concomitant use of oral, systemically absorbed corticosteroids at baseline, concomitant use of immunomodulators at baseline, prior exposure to biologics, and treatment group.	
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least Squares Mean Difference
Point estimate	-31
Confidence interval	
level	90 %
sides	2-sided
lower limit	-76
upper limit	15

Variability estimate	Standard error of the mean
Dispersion value	27.4

Secondary: Change From Baseline in CDAI Scores at Week 24

End point title	Change From Baseline in CDAI Scores at Week 24

End point description:

The CDAI score is used to quantify the symptoms of participants with Crohn's Disease. The score ranges from 0 to 600. A score of < 150 indicates remission. A higher score indicates more severe disease. Diff in LSM were from ANCOVA model. A negative change from baseline indicates improvement. Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	32	18	
Units: score on scale				
least squares mean (standard error)	-86 (± 24.1)	-71 (± 22.8)	-66 (± 26.7)	

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo

Statistical analysis description:

Diff in LSM, and its 90% CI were from ANCOVA model adjusted by baseline segmental MaRIA score, concomitant use of oral, systemically absorbed corticosteroids at baseline, concomitant use of immunomodulators at baseline, prior exposure to biologics, and treatment group.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least Squares Mean Difference
Point estimate	-20
Confidence interval	
level	90 %
sides	2-sided
lower limit	-68
upper limit	28
Variability estimate	Standard error of the mean
Dispersion value	28.7

Statistical analysis title	Filgotinib 100 mg vs Placebo

Statistical analysis description:

Diff in LSM, and its 90% CI were from ANCOVA model adjusted by baseline segmental MaRIA score, concomitant use of oral, systemically absorbed corticosteroids at baseline, concomitant use of immunomodulators at baseline, prior exposure to biologics, and treatment group.

Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least Squares Mean Difference
Point estimate	-5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-52
upper limit	42
Variability estimate	Standard error of the mean
Dispersion value	28

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-Cause Mortality: First dose date up to last dose date (maximum: 28.7 weeks) plus 59 days; Adverse Events: First dose date up to last dose date (maximum: 28.7 weeks) plus 30 days

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Filgotinib 200 mg

Reporting group description:

Filgotinib 200 mg tablet + PTM filgotinib 100 mg tablet orally once daily up to 27 weeks.

Reporting group title	Filgotinib 100 mg

Reporting group description:

Filgotinib 100 mg tablet + PTM filgotinib 200 mg tablet orally once daily up to 26.3 weeks.

Reporting group title	Placebo

Reporting group description:

PTM filgotinib 200 mg tablet +PTM filgotinib 100 mg tablet orally once daily up to 28.7 weeks.

Serious adverse events	Filgotinib 200 mg	Filgotinib 100 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 28 (14.29%)	7 / 32 (21.88%)	0 / 18 (0.00%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	2 / 28 (7.14%)	4 / 32 (12.50%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	2 / 28 (7.14%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			

subjects affected / exposed	0 / 28 (0.00%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 28 (0.00%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Filgotinib 200 mg	Filgotinib 100 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 28 (71.43%)	24 / 32 (75.00%)	13 / 18 (72.22%)
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 28 (10.71%)	1 / 32 (3.13%)	1 / 18 (5.56%)
occurrences (all)	3	1	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 28 (7.14%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	2	1	0
Asthenia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Pyrexia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Influenza like illness			
subjects affected / exposed	0 / 28 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1

Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 28 (3.57%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
Sinus congestion			
subjects affected / exposed	0 / 28 (0.00%)	1 / 32 (3.13%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 28 (3.57%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 28 (7.14%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 28 (14.29%)	4 / 32 (12.50%)	2 / 18 (11.11%)
occurrences (all)	4	4	2
Dizziness			
subjects affected / exposed	1 / 28 (3.57%)	2 / 32 (6.25%)	2 / 18 (11.11%)
occurrences (all)	1	2	2
Tremor			
subjects affected / exposed	0 / 28 (0.00%)	1 / 32 (3.13%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Paraesthesia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 28 (3.57%)	2 / 32 (6.25%)	1 / 18 (5.56%)
occurrences (all)	1	2	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 28 (0.00%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	5 / 28 (17.86%)	6 / 32 (18.75%)	1 / 18 (5.56%)
occurrences (all)	5	6	2
Crohn's disease			
subjects affected / exposed	4 / 28 (14.29%)	6 / 32 (18.75%)	2 / 18 (11.11%)
occurrences (all)	4	6	2
Nausea			
subjects affected / exposed	5 / 28 (17.86%)	3 / 32 (9.38%)	1 / 18 (5.56%)
occurrences (all)	6	3	3
Vomiting			
subjects affected / exposed	1 / 28 (3.57%)	2 / 32 (6.25%)	2 / 18 (11.11%)
occurrences (all)	1	2	2
Abdominal distension			
subjects affected / exposed	2 / 28 (7.14%)	1 / 32 (3.13%)	1 / 18 (5.56%)
occurrences (all)	2	1	1
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 28 (3.57%)	2 / 32 (6.25%)	1 / 18 (5.56%)
occurrences (all)	1	2	1
Diarrhoea			
subjects affected / exposed	0 / 28 (0.00%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Dyspepsia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 32 (3.13%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Proctalgia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Rectal haemorrhage			
subjects affected / exposed	1 / 28 (3.57%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	2
Anal incontinence			
subjects affected / exposed	0 / 28 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 28 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1

Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 28 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 28 (3.57%)	1 / 32 (3.13%)	1 / 18 (5.56%)
occurrences (all)	1	1	1
Muscle spasms			
subjects affected / exposed	0 / 28 (0.00%)	1 / 32 (3.13%)	2 / 18 (11.11%)
occurrences (all)	0	1	2
Pain in extremity			
subjects affected / exposed	0 / 28 (0.00%)	2 / 32 (6.25%)	1 / 18 (5.56%)
occurrences (all)	0	2	1
Arthralgia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 32 (3.13%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Sacroiliitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Infections and infestations			
Sinusitis			
subjects affected / exposed	4 / 28 (14.29%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	4	0	1
Influenza			
subjects affected / exposed	3 / 28 (10.71%)	1 / 32 (3.13%)	0 / 18 (0.00%)
occurrences (all)	3	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 28 (0.00%)	4 / 32 (12.50%)	0 / 18 (0.00%)
occurrences (all)	0	4	0
Urinary tract infection			

subjects affected / exposed	1 / 28 (3.57%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	1	3	0
Ear infection			
subjects affected / exposed	1 / 28 (3.57%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)	2 / 32 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Gastroenteritis viral			
subjects affected / exposed	0 / 28 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	0 / 28 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 28 (7.14%)	0 / 32 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 32 (3.13%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Hypocalcaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Malnutrition			
subjects affected / exposed	0 / 28 (0.00%)	0 / 32 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 December 2016	• Added a data monitoring committee (DMC) • Updated secondary endpoints language for consistency with the secondary objectives and the definition of terms • Moved definitions of efficacy related to MaRIA scores from the study objectives to the definition of terms • Added requirement to assess coagulation parameters for instances where aspartate transaminase (AST) or alanine transaminase (ALT) is >3 * upper limit of normal (ULN) • Extended requirement for maintaining a stable prescribed dose of corticosteroids prior to randomization • Updated requirements for storage and handling of study drugs • Added natalizumab, leflunomide, and lymphocyte-depleting therapies to the list of prohibited concomitant medications • Provided a rationale for the exclusion of potent P-gp inducers • Deleted appendix 5 and renumbered subsequent appendices. Moved information pertaining to subject preparation for MRE acquisition from appendix 5 to Section 6. Removed technical aspects of MRE acquisition • Added hepatitis B virus (HBV) surface antibody test and HBV core antibody test to screening • Removed details of MaRIA segmental score calculation from appendix 5
26 June 2017	• Added study duration • Updated background information with emerging relevant clinical data and to ensure consistency with Edition 12 of the Investigator's Brochure for filgotinib • Added formula for creatinine clearance (CLcr) calculation • Updated biomarker language to align with Gilead's current protocol template • Updated inclusion criterion to add ustekinumab as possible therapy of previously demonstrated inadequate response • Updated inclusion criterion to clarify that QuantiFERON tuberculosis testing may not berepeated except in the case of a single repeat for indeterminate results • Added a new inclusion criterion to ensure standard of care colorectal cancer screening for patient population • Updated exclusion criteria to remove tattoo as a contraindication to MRE examination • Updated exclusion criteria to clarify exclusion of subjects with subtotal colectomy • Updated exclusion criteria to clarify the required washout period before entry of subjects who have been previously treated with ustekinumab • Added guidance for missed doses • Added guidance for initiation of new induction therapies prior to screening • Added instructions for budesonide taper • Added detailed descriptions of key assessments • Updated safety reporting language to align with Gilead's current protocol template • Added wording to the informed consent process to ensure investigators counsel male participants on the associated risks of male infertility • Added urinalysis to Week 24 • Separated fasting lipids from serum chemistry • Defined the duration of fasting • Removed fasting requirement from screening • Updated Appendix 7 based on findings of a drug-drug interaction (DDI) study for filgotinib and hormonal contraceptives and to clarify the definitions of childbearing potential

04 February 2020	• Updated study secondary and exploratory endpoints • Updates were made to include discontinuation criteria for thromboembolic events at the request of US Food and Drug Administration (FDA) • Included a criterion to trigger an ad hoc DMC meeting at the request of the US FDA • Added description of a cardiovascular safety endpoint adjudication committee (CVEAC) that Gilead established at the request of the US FDA • Included new guidance for HBV deoxyribonucleic acid (DNA) screening and surveillance

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported