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

Summary

EudraCT number	2016-003153-15
Trial protocol	GB HU CZ DE PL ES AT BE IT
Global end of trial date	17 February 2021

Results information

Result version number	v1
This version publication date	08 March 2022
First version publication date	08 March 2022

Trial information

Trial identification

Sponsor protocol code	GS-US-419-4016

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03077412
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	17 February 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 January 2021
Global end of trial reached?	Yes
Global end of trial date	17 February 2021
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 as compared to placebo in establishing combined fistula response at 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	06 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	Canada: 5
Country: Number of subjects enrolled	United States: 27
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Austria: 8
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Italy: 1
Worldwide total number of subjects	57
EEA total number of subjects	24

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)	56
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Europe and the United States. The first participant was screened on 06 April 2017. The last study visit occurred on 17 February 2021.

Pre-assignment

Screening details:

106 participants were screened. Participants who were non-responders, met disease worsening criteria or completed all procedures per protocol, were offered the option to continue into a separate Long Term Extension (LTE) study (GS-US-419-3896; NCT02914600), if deemed appropriate by the investigator.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Filgotinib 200 mg

Arm description:

Participants received filgotinib 200 milligrams (mg) and placebo to match (PTM) filgotinib 100 mg, once daily for 24 weeks.

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

Dosage and administration details:

200 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 100 mg administered once daily

Arm title	Filgotinib 100 mg

Arm description:

Participants received filgotinib 100 mg and PTM filgotinib 200 mg, once daily for 24 weeks.

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

Dosage and administration details: 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	
Arm title	Placebo
Arm description: Participants received PTM filgotinib 200 mg and PTM filgotinib 100 mg, once daily for 24 weeks.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: PTM filgotinib 100 mg administered once daily	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: PTM filgotinib 200 mg administered once daily	

Number of subjects in period 1	Filgotinib 200 mg	Filgotinib 100 mg	Placebo
Started	17	25	15
Completed	14	12	6
Not completed	3	13	9
Withdrew Consent	-	2	-
Adverse Event	1	2	2
Non-Responder at Week 10	1	5	3
Protocol-Specified Disease Worsening	1	3	3
Investigator's Discretion	-	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Filgotinib 200 mg
Reporting group description:	
Participants received filgotinib 200 milligrams (mg) and placebo to match (PTM) filgotinib 100 mg, once daily for 24 weeks.	
Reporting group title	Filgotinib 100 mg
Reporting group description:	
Participants received filgotinib 100 mg and PTM filgotinib 200 mg, once daily for 24 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received PTM filgotinib 200 mg and PTM filgotinib 100 mg, once daily for 24 weeks.	

Reporting group values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo
Number of subjects	17	25	15
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	39	41	39
standard deviation	± 11.2	± 14.0	± 11.8
Gender categorical Units: Subjects			
Female	9	10	4
Male	8	15	11
Race			
Not Permitted = local regulators did not allow collection of race information.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	2	0
Black or African American	1	2	1
Native Hawaiian or Pacific Islander	0	0	0
White	15	19	14
Other	0	0	0
Not Permitted	1	2	0
Ethnicity			
Not Permitted = local regulators did not allow collection of ethnicity information.			
Units: Subjects			
Not Hispanic or Latino	17	23	15
Hispanic or Latino	0	1	0
Not Permitted	0	1	0

Reporting group values	Total		
Number of subjects	57		

Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- 		
Gender categorical Units: Subjects			
Female	23		
Male	34		
Race			
Not Permitted = local regulators did not allow collection of race information.			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	2		
Black or African American	4		
Native Hawaiian or Pacific Islander	0		
White	48		
Other	0		
Not Permitted	3		
Ethnicity			
Not Permitted = local regulators did not allow collection of ethnicity information.			
Units: Subjects			
Not Hispanic or Latino	55		
Hispanic or Latino	1		
Not Permitted	1		

End points

End points reporting groups

Reporting group title	Filgotinib 200 mg
Reporting group description:	
Participants received filgotinib 200 milligrams (mg) and placebo to match (PTM) filgotinib 100 mg, once daily for 24 weeks.	
Reporting group title	Filgotinib 100 mg
Reporting group description:	
Participants received filgotinib 100 mg and PTM filgotinib 200 mg, once daily for 24 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received PTM filgotinib 200 mg and PTM filgotinib 100 mg, once daily for 24 weeks.	

Primary: Percentage of Participants who Achieved Combined Fistula Response at Week 24

End point title	Percentage of Participants who Achieved Combined Fistula Response at Week 24
End point description:	
Combined fistula response at Week 24 was defined as reduction of greater than or equal to (≥) 1 from baseline in the number of draining external perianal fistula openings that were present at baseline, and absence of fluid collections > 1 centimeter (cm) on magnetic resonance imaging (MRI) pelvis at Week 24, among participants with at least 1 draining external perianal fistula opening at baseline. Participants in Full Analysis Set (all the randomized participants who received at least 1 dose of the study drug) with at least 1 draining external perianal fistula opening at baseline were analyzed.	
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	17	24	12	
Units: percentage of participants				
number (confidence interval 90%)	47.1 (26.0 to 68.9)	29.2 (14.6 to 47.9)	25.0 (7.2 to 52.7)	

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo
Statistical analysis description:	
The 90% exact CI was calculated based on binomial distribution (Clopper-Pearson method).	
Comparison groups	Filgotinib 200 mg v Placebo

Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	22.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.9
upper limit	50

Statistical analysis title	Filgotinib 100 mg vs Placebo
Statistical analysis description:	
The 90% exact CI was calculated based on binomial distribution (Clopper-Pearson method).	
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	36
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	-26.5
upper limit	34.3

Secondary: Percentage of Participants Who Achieved Combined Fistula Remission at Week 24

End point title	Percentage of Participants Who Achieved Combined Fistula Remission at Week 24
End point description:	
Combined fistula remission at Week 24 was defined as perianal fistula closure of all external openings that were draining at baseline, and absence of fluid collections > 1 cm on MRI pelvis at Week 24, among participants with at least 1 draining external perianal fistula opening at baseline. Participants in the Full Analysis Set with at least 1 draining external perianal fistula opening 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	17	24	12	
Units: percentage of participants				
number (confidence interval 90%)	47.1 (26.0 to 68.9)	25.0 (11.5 to 43.5)	16.7 (3.0 to 43.8)	

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo
Statistical analysis description:	
The 90% exact CI was calculated based on binomial distribution (Clopper-Pearson method).	
Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	30.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.3
upper limit	57.3

Statistical analysis title	Filgotinib 100 mg vs Placebo
Statistical analysis description:	
The 90% exact CI was calculated based on binomial distribution (Clopper-Pearson method).	
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Risk Difference in Proportions
Point estimate	8.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-22.5
upper limit	38.1

Secondary: Time to Clinical Fistula Response up to Week 24

End point title	Time to Clinical Fistula Response up to Week 24

End point description:

Time to clinical fistula response was defined as the time interval in days from date of first dosing of study drug to the first observation (during scheduled or unscheduled clinical visits) when ≥ 1 of the

draining external perianal fistula openings that were present at baseline achieved perianal fistula closure, among participants with at least 1 draining external perianal fistula opening at baseline. Participants not known to have a clinical fistula response had their clinical fistula response time censored at the last time that lack of clinical fistula response was documented. Participants in the Full Analysis Set with at least 1 draining external perianal fistula opening at baseline were analyzed.

End point type	Secondary

End point timeframe:

Time from treatment start to first visit when ≥ 1 of the draining external perianal fistula openings that were present at baseline achieved perianal fistula closure up to 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	17	24	12	
Units: days				
median (confidence interval 90%)	15 (15 to 28)	16 (15 to 71)	35.5 (15 to 71)	

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo
Statistical analysis description:	
Hazard ratio was derived from Cox Proportional-Hazards model.	
Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.26
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.64
upper limit	2.49

Statistical analysis title	Filgotinib 100 mg vs Placebo
Statistical analysis description:	
Hazard ratio was derived from Cox Proportional-Hazards model.	
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.47
upper limit	1.75

Secondary: Time to Clinical Fistula Remission up to Week 24

End point title	Time to Clinical Fistula Remission up to Week 24

End point description:

Time to clinical fistula remission was defined as the time interval in days from date of first dosing of study drug to the first observation (during schedule or unscheduled clinical visits) of perianal fistula closure of all external openings that were draining at baseline, among participants with at least 1 draining external perianal fistula opening at baseline. Participants not known to have a clinical fistula remission had their clinical fistula remission time censored at the last time that lack of clinical fistula remission was documented. Participants in the Full Analysis Set with at least 1 draining external perianal fistula opening at baseline were analyzed. 99999 signifies higher bound was not available based on the data.

End point type	Secondary

End point timeframe:

Time from treatment start to first visit when perianal fistula closure takes place of all external openings that were draining at baseline up to 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	17	24	12	
Units: days				
median (confidence interval 90%)	15 (15 to 70)	29 (16 to 74)	71 (26 to 99999)	

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo

Statistical analysis description:

Hazard ratio was derived from Cox Proportional-Hazards model.

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.87
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.87
upper limit	4.01

Statistical analysis title	Filgotinib 100 mg vs Placebo
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.37
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.65
upper limit	2.92

Secondary: Percentage of Participants who Achieved Proctitis Remission at Week 24

End point title	Percentage of Participants who Achieved Proctitis Remission at Week 24

End point description:

The simple endoscopic score for Crohn's disease (SES-CD) score evaluates 4 endoscopic variables (ulcer size, ulcerated surface, affected surface, and presence of narrowings). The total SES-CD is calculated as the sum of the 4 variables for the required bowel segment. Values are given to each variable and for every examined bowel segment. The SES-CD size of ulcer subscore ranges from 0 (none) to 3 (very large) and for ulcerated surface subscore ranges from 0 (none) to 3 (>30 % of affected area). Higher value of the subscore indicates disease worsening. Proctitis remission at Week 24 was defined as a proctitis SES-CD score (sum of ulcer size and ulcerated surface SES-CD endoscopy subscores for the rectum and anal canal) of 0 assessed by centrally read flexible sigmoidoscopy at Week 24. Moderately to Severely Active Proctitis defined as proctitis SES-CD Score > 2. Participants in the Full Analysis Set who had moderately to severely active proctitis 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	13	7	
Units: percentage of participants				
number (confidence interval 90%)	10.0 (0.5 to 39.4)	15.4 (2.8 to 41.0)	28.6 (5.3 to 65.9)	

Statistical analyses

Statistical analysis title	Filgotinib 200 mg vs Placebo

Statistical analysis description:

The 90% exact CI was calculated based on binomial distribution (Clopper-Pearson method).

Comparison groups	Filgotinib 200 mg v Placebo
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	-18.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-55.6
upper limit	21.3

Statistical analysis title	Filgotinib 100 mg vs Placebo
Statistical analysis description:	
The 90% exact CI was calculated based on binomial distribution (Clopper-Pearson method).	
Comparison groups	Filgotinib 100 mg v Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk Difference in Proportions
Point estimate	-13.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-51
upper limit	24.1

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: First dose date up to 24 weeks plus 30 days; All-Cause Mortality: Randomization up to 46 months.

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 Set included all participants who were randomized in the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Filgotinib 200 mg

Reporting group description:

Participants received filgotinib 200 mg and PTM filgotinib 100 mg, once daily for up to Week 26.

Reporting group title	Placebo

Reporting group description:

Participants received PTM filgotinib 200 mg and PTM filgotinib 100 mg, once daily for up to Week 27.9.

Reporting group title	Filgotinib 100 mg

Reporting group description:

Participants received filgotinib 100 mg and PTM filgotinib 200 mg, once daily for up to Week 29.3.

Serious adverse events	Filgotinib 200 mg	Placebo	Filgotinib 100 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 17 (29.41%)	1 / 15 (6.67%)	2 / 25 (8.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	2 / 25 (8.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal stenosis			

subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suspected COVID-19			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vulval abscess			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (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

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

Non-serious adverse events	Filgotinib 200 mg	Placebo	Filgotinib 100 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 17 (76.47%)	11 / 15 (73.33%)	14 / 25 (56.00%)
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 17 (17.65%)	0 / 15 (0.00%)	3 / 25 (12.00%)
occurrences (all)	3	0	3
Pyrexia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Crying			

subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Exercise tolerance decreased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Medical device pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 17 (5.88%)	1 / 15 (6.67%)	2 / 25 (8.00%)
occurrences (all)	1	1	3
Pharyngeal hypoaesthesia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 17 (5.88%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	1	1	0
Fall			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Muscle strain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Road traffic accident			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Skin laceration			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0

Sunburn			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 17 (0.00%)	0 / 15 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Tachycardia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 17 (5.88%)	1 / 15 (6.67%)	1 / 25 (4.00%)
occurrences (all)	1	1	1
Dysaesthesia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Mental impairment			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Taste disorder			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Photophobia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Visual impairment			

subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Anal fistula			
subjects affected / exposed	2 / 17 (11.76%)	2 / 15 (13.33%)	2 / 25 (8.00%)
occurrences (all)	2	3	2
Crohn's disease			
subjects affected / exposed	2 / 17 (11.76%)	1 / 15 (6.67%)	2 / 25 (8.00%)
occurrences (all)	2	1	2
Nausea			
subjects affected / exposed	2 / 17 (11.76%)	1 / 15 (6.67%)	2 / 25 (8.00%)
occurrences (all)	2	1	2
Abdominal distension			
subjects affected / exposed	1 / 17 (5.88%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	1	1	0
Abdominal pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	2
Diarrhoea			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	1 / 25 (4.00%)
occurrences (all)	2	0	1
Vomiting			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Abdominal pain upper			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Faeces discoloured			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Food poisoning			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0

Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia oral			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Proctalgia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 17 (5.88%)	2 / 15 (13.33%)	1 / 25 (4.00%)
occurrences (all)	1	2	2
Alopecia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Onychoclasis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Skin lesion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 17 (17.65%)	0 / 15 (0.00%)	2 / 25 (8.00%)
occurrences (all)	3	0	2
Back pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Muscle spasms			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			

Influenza			
subjects affected / exposed	3 / 17 (17.65%)	2 / 15 (13.33%)	1 / 25 (4.00%)
occurrences (all)	3	2	1
Nasopharyngitis			
subjects affected / exposed	2 / 17 (11.76%)	2 / 15 (13.33%)	2 / 25 (8.00%)
occurrences (all)	2	2	2
Anal abscess			
subjects affected / exposed	3 / 17 (17.65%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	3	1	0
Oral herpes			
subjects affected / exposed	2 / 17 (11.76%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	2	1	0
Abscess limb			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Ear infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Pharyngitis streptococcal			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Abscess			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Abscess soft tissue			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Anal fungal infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Fungal skin infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0

Gastroenteritis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Viral infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 15 (6.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Malnutrition			
subjects affected / exposed	1 / 17 (5.88%)	0 / 15 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 January 2017	Amendment 1: •Updated projected study centers based on recent site selection metrics •Added a secondary objective for the evaluation of proctitis remission • Updates made to 3 exploratory objectives •Added randomization stratum of proctitis status •Removed inclusion criterion of perianal CDAI(PDAI)>4 •Clarified inclusion criterion around the acceptability of non-perianal fistulae and concurrent noncutting perianal seton(s) removal prior to randomization •Added inclusion of participants that had previously demonstrated treatment failure to a 4-week regimen of antibiotics for the treatment of perianal fistulae •Removed corticosteroids and vedolizumab from the inclusion criterion for defining participants as inadequate clinical responders •Updated to clarify that administration of stable doses of permitted concomitant medications was mandatory •Extended requirement for stable doses of corticosteroid therapy prior to randomization •Decreased the maximum dose permitted for prednisone (or equivalent) •Removed inclusion criterion around participant willingness and ability to take antibiotic treatment for perianal fistulizing Crohn's disease (CD) and > 3 draining fistula of any type •Updated exclusionary CD activity index (CDAI) value •Clarified that participants must have an intact rectum in order to assess active proctitis at baseline •Added flexible sigmoidoscopy procedure and Simple Endoscopic Score (SES)-CD scoring •Clarified LTE study eligibility requirements for participants who met responder criteria •Added text to clarify when study and/or study drug discontinuation was mandatory •Added a data monitoring committee •Updated table of definitions to include all new definitions in alignment with changes to the objectives of the study •Updated background section of the protocol, including rationale for this study •Added a secondary efficacy end point of the proportion of participants achieving proctitis remission at Week 24

26 June 2017	Amendment 2: • Added ClinicalTrials.gov identifier • Updated secondary objectives and end points to eliminate redundancy • 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 calculation • Updated biomarker language to align with Gilead's current protocol template • Updated inclusion criterion to clarify that QuantiFERON TB testing could not be repeated 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 7 to remove tattoo as a contraindication to MRI examination • Updated exclusion criteria to clarify the required washout period before entry of participants who had 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 counseled male participants on the associated risks of male infertility • Removed PDAI from screening • Added urinalysis to Week 24 • Separated fasting lipids from serum chemistry • Defined the duration of fasting • Removed fasting requirement from screening • Appendix 9 updated based on findings of drug-drug interaction study for filgotinib and hormonal contraceptives and to clarify the definitions of childbearing potential
11 October 2018	Amendment 3: • Further clarified the eligible participant population via updates to study inclusion/exclusion criteria • Ensured study end points were evaluable for early terminating participants by addition of assessments at the early termination (ET) visit • Updated study director and medical monitor contact information • Updated Data Monitoring Committee meeting schedule to reflect the committee charter
11 April 2019	Amendment 4: • Incorporated criteria for the assessment of non-response of perianal fistulae using patient reported symptom subscores of the PDAI • Allowed the concurrent use of vedolizumab therapy • Expanded the definition of dual refractory male participants in the United States • Replaced a stratification factor • Added an interim futility analysis for efficacy • Clarified that endoscopic assessment of anal canal was being conducted as part of the centrally read flexible sigmoidoscopy • Added a new exploratory objective for the study • Added a new exploratory end point for the study

04 February 2020	Amendment 5: • Included additional criteria for luminal disease non-response • Included discontinuation criteria for thromboembolic events at the request of the United States Food and Drug Administration (US FDA) • Included a criterion to trigger an ad hoc DMC meeting at the request of the US FDA • Described a cardiovascular safety end point adjudication committee (CVEAC) that Gilead established at the request of the FDA • Included new guidance for hepatitis B virus (HBV) deoxyribonucleic acid (DNA) screening and surveillance

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported