Clinical trial results:
A Phase 2a, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, Tolerability and Pharmacokinetics of PF-06687234 as Add-On Therapy to Infliximab in Active Ulcerative Colitis Subjects Who Are Not in Remission (Build UC)

Summary

EudraCT number	2017-002108-28
Trial protocol	BE DE ES IT
Global end of trial date	07 January 2021

Results information

Result version number	v1 (current)
This version publication date	19 November 2021
First version publication date	19 November 2021

Trial information

Trial identification

Sponsor protocol code	B7581002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03269695
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 18007181021, ClinicalTrials.gov_Inquiries@pfizer.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	07 January 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 January 2021
Global end of trial reached?	Yes
Global end of trial date	07 January 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This study was the first to assess PF 06487234 as add on therapy to infliximab, intravenous (IV) regimen in subjects with active ulcerative colitis (UC). The study was terminated after an interim analysis, due to efficacy being considered unlikely to meet the projected target.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 December 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	Belgium: 1
Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Korea, Republic of: 2
Country: Number of subjects enrolled	Saudi Arabia: 1
Country: Number of subjects enrolled	Serbia: 1
Country: Number of subjects enrolled	Turkey: 1
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	20
EEA total number of subjects	4

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)	17
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 46 subjects were screened, of whom 20 were randomized and treated (10 subjects each in the Placebo + Infliximab and PF-06687234 20 mg + Infliximab treatment groups). Fifteen subjects completed the treatment.

Pre-assignment

Screening details:

Subjects with active histologic UC (histologic) for >= 4 months, and on a stable dose 5 to 10 milligram/kilogram (mg/kg) of Remicade, or protocol specified infliximab biosimilars for a minimum of 14 weeks prior to study entry with no anticipation of need for change in infliximab treatment regimen throughout the study were enrolled.

Period 1

Period 1 title	PF-06687234 Treatment Period (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	Placebo + Infliximab

Arm description:

Placebo for PF06687234 was administered as subcutaneous injection on Day 1, Week 1 (Day 8), Week 2 (Day 15), Week 3 (Day 22), Week 4 (Day 29), Week 5 (Day 36), Week 6 (Day 43), Week 7 (Day 50), Week 8 (Day 57), Week 9 (Day 64), Week 10 (Day 71) and Week 11 (Day 78) for a total 12 doses. Remicade or protocol specified infliximab biosimilar was administered as an IV infusion on Day 1, Week 8 and Week 16 for a total of 3 doses for subjects on infliximab every 8 weeks, and Day 1, Week 6, Week 12 and Week 18 for subjects on infliximab every 6 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo for PF-06687234
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

PF-06687234 0 mg/vial

Investigational medicinal product name	Infliximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Infliximab 100 mg/vial

Arm title	PF-06687234 20 mg + Infliximab

Arm description:

PF-06687234 was administered as a 20 mg subcutaneous injection on Day 1, Week 1 (Day 8), Week 2 (Day 15), Week 3 (Day 22), Week 4 (Day 29), Week 5 (Day 36), Week 6 (Day 43), Week 7 (Day 50), Week 8 (Day 57), Week 9 (Day 64), Week 10 (Day 71) and Week 11 (Day 78) for a total 12 doses. Remicade or protocol specified infliximab biosimilar was administered as an IV infusion on Day 1, Week 8 and Week 16 for a total of 3 doses for subjects on infliximab every 8 weeks, and Day 1, Week 6, Week 12 and Week 18 for subjects on infliximab every 6 weeks.

Arm type	Experimental

Investigational medicinal product name	Infliximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
Infliximab 100 mg/vial

Investigational medicinal product name	PF-06687234
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:
PF-06687234 20 mg/vial

Number of subjects in period 1	Placebo + Infliximab	PF-06687234 20 mg + Infliximab
Started	10	10
Completed	8	7
Not completed	2	3
Consent withdrawn by subject	-	1
Adverse event, non-fatal	2	1
Lack of efficacy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo + Infliximab
Reporting group description:	
Placebo for PF06687234 was administered as subcutaneous injection on Day 1, Week 1 (Day 8), Week 2 (Day 15), Week 3 (Day 22), Week 4 (Day 29), Week 5 (Day 36), Week 6 (Day 43), Week 7 (Day 50), Week 8 (Day 57), Week 9 (Day 64), Week 10 (Day 71) and Week 11 (Day 78) for a total 12 doses. Remicade or protocol specified infliximab biosimilar was administered as an IV infusion on Day 1, Week 8 and Week 16 for a total of 3 doses for subjects on infliximab every 8 weeks, and Day 1, Week 6, Week 12 and Week 18 for subjects on infliximab every 6 weeks.	
Reporting group title	PF-06687234 20 mg + Infliximab
Reporting group description:	
PF-06687234 was administered as a 20 mg subcutaneous injection on Day 1, Week 1 (Day 8), Week 2 (Day 15), Week 3 (Day 22), Week 4 (Day 29), Week 5 (Day 36), Week 6 (Day 43), Week 7 (Day 50), Week 8 (Day 57), Week 9 (Day 64), Week 10 (Day 71) and Week 11 (Day 78) for a total 12 doses. Remicade or protocol specified infliximab biosimilar was administered as an IV infusion on Day 1, Week 8 and Week 16 for a total of 3 doses for subjects on infliximab every 8 weeks, and Day 1, Week 6, Week 12 and Week 18 for subjects on infliximab every 6 weeks.	

Reporting group values	Placebo + Infliximab	PF-06687234 20 mg + Infliximab	Total
Number of subjects	10	10	20
Age Categorical Units: Subjects			
18-44 Years	5	6	11
45-64 Years	2	4	6
≥ 65 Years	3	0	3
Age Continuous Units: Years			
arithmetic mean	44.6	44.5	
standard deviation	± 21.11	± 12.44	-
Sex: Female, Male Units: Subjects			
Female	3	4	7
Male	7	6	13
Race/Ethnicity, Customized Units: Subjects			
White	8	8	16
Asian	2	2	4
Race/Ethnicity, Customized Units: Subjects			
Not Hispanic or Latino	10	10	20
Age Continuous Units: Years			
median	44.5	43.5	
full range (min-max)	20 to 73	20 to 64	-

End points

End points reporting groups

Reporting group title	Placebo + Infliximab

Reporting group description:

Placebo for PF06687234 was administered as subcutaneous injection on Day 1, Week 1 (Day 8), Week 2 (Day 15), Week 3 (Day 22), Week 4 (Day 29), Week 5 (Day 36), Week 6 (Day 43), Week 7 (Day 50), Week 8 (Day 57), Week 9 (Day 64), Week 10 (Day 71) and Week 11 (Day 78) for a total 12 doses. Remicade or protocol specified infliximab biosimilar was administered as an IV infusion on Day 1, Week 8 and Week 16 for a total of 3 doses for subjects on infliximab every 8 weeks, and Day 1, Week 6, Week 12 and Week 18 for subjects on infliximab every 6 weeks.

Reporting group title	PF-06687234 20 mg + Infliximab

Reporting group description:

PF-06687234 was administered as a 20 mg subcutaneous injection on Day 1, Week 1 (Day 8), Week 2 (Day 15), Week 3 (Day 22), Week 4 (Day 29), Week 5 (Day 36), Week 6 (Day 43), Week 7 (Day 50), Week 8 (Day 57), Week 9 (Day 64), Week 10 (Day 71) and Week 11 (Day 78) for a total 12 doses. Remicade or protocol specified infliximab biosimilar was administered as an IV infusion on Day 1, Week 8 and Week 16 for a total of 3 doses for subjects on infliximab every 8 weeks, and Day 1, Week 6, Week 12 and Week 18 for subjects on infliximab every 6 weeks.

Primary: Percentage of Subjects in Modified Clinical Remission at Week 12 (Traditional Mayo Endoscopic Subscore <=1, Observed Cases)

End point title	Percentage of Subjects in Modified Clinical Remission at Week 12 (Traditional Mayo Endoscopic Subscore <=1, Observed Cases)

End point description:

The Mayo score consists of 4 subscores (Endoscopic, stool frequency, rectal bleeding and Physician's global assessment [PGA]), each graded 0 to 3 with the higher score indicating more severe disease activity. Modified clinical remission is defined as a modified total Mayo Score (total Mayo score excluding the PGA subscore) <=2, no individual subscore >1, traditional endoscopic subscore <=1 (where mild friability was scored as of 1; moderate or severe friability was scored as 2) and rectal bleeding subscore = 0. All subjects who had at least one dose of the randomized treatment were included in the analysis population. Subjects with missing values were handled by observed case approach (the missing data were used as is). The number of subjects with observed data were 8 for the Placebo + Infliximab arm and 7 for PF-06687234 20 mg + Infliximab arm. The percentage of subjects achieving modified clinical remission was calculated based on the number of subjects with observed data.

End point type	Primary

End point timeframe:

Week 12

End point values	Placebo + Infliximab	PF-06687234 20 mg + Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Percentage of subjects (%)				
number (confidence interval 95%)	12.5 (0.6 to 50.0)	14.3 (0.7 to 55.4)		

Statistical analyses

Statistical analysis title	Treatment Difference Between 2 Arms
Comparison groups	Placebo + Infliximab v PF-06687234 20 mg + Infliximab
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Chan and Zhang (1999)
Parameter estimate	Treatment difference
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-41
upper limit	47.2

Primary: Percentage of Subjects in Modified Clinical Remission at Week 12 (Traditional Mayo Endoscopic Subscore <=1, Treatment Failure Approach)

End point title	Percentage of Subjects in Modified Clinical Remission at Week 12 (Traditional Mayo Endoscopic Subscore <=1, Treatment Failure Approach)

End point description:

The Mayo score consists of 4 subscores (Endoscopic, stool frequency, rectal bleeding and Physician's global assessment [PGA]), each graded 0 to 3 with the higher score indicating more severe disease activity. Modified clinical remission is defined as a modified total Mayo Score (total Mayo score excluding the PGA subscore) <=2, no individual subscore > 1, traditional endoscopic subscore <=1 (where mild friability was scored as of 1; moderate or severe friability was scored as 2) and rectal bleeding subscore = 0. All subjects who had received at least one dose of the randomized treatment were included in the analysis population. Subjects with missing values were handled by treatment failure approach (subjects who had missing value for any reasons were considered as treatment failures).

End point type	Primary

End point timeframe:

Week 12

End point values	Placebo + Infliximab	PF-06687234 20 mg + Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Percentage of subjects (%)				
number (confidence interval 95%)	10 (0.5 to 44.4)	10 (0.5 to 44.4)		

Statistical analyses

Statistical analysis title	Treatment Difference Between 2 Arms
Comparison groups	Placebo + Infliximab v PF-06687234 20 mg + Infliximab

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Chan and Zhang (1999)
Parameter estimate	Treatment difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37
upper limit	37

Primary: Percentage of Subjects in Modified Clinical Remission at Week 12 (Modified Mayo Endoscopy Subscore = 0 or 1, Observed Cases)

End point title	Percentage of Subjects in Modified Clinical Remission at Week 12 (Modified Mayo Endoscopy Subscore = 0 or 1, Observed Cases)

End point description:

The Mayo score consists of 4 subscores (Endoscopic, stool frequency, rectal bleeding and Physician's global assessment), each graded 0 to 3 with the higher score indicating more severe disease activity. Modified clinical remission is defined as a modified total Mayo Score (total Mayo score excluding the PGA subscore) with modified endoscopic subscore = 0 or 1 (where any friability was scored as a mayo endoscopic subscore of 2), stool frequency subscore = 0 or 1, and rectal bleeding subscore = 0. All subjects who had received at least one dose of the randomized treatment were included in the analysis population. Subjects with missing values were handled by observed case approach (the missing data were used as is). The number of subjects with observed data were 8 for the Placebo + Infliximab arm and 7 for PF-06687234 20mg + Infliximab arm. The percentage of subjects achieving modified clinical remission was calculated based on the number of subjects with observed data.

End point type	Primary

End point timeframe:

Week 12

End point values	Placebo + Infliximab	PF-06687234 20 mg + Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Percentage of subjects (%)				
number (confidence interval 95%)	0 (0.0 to 34.9)	14.3 (0.7 to 55.4)		

Statistical analyses

Statistical analysis title	Treatment Difference Between 2 Arms
Comparison groups	Placebo + Infliximab v PF-06687234 20 mg + Infliximab

Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.47
Method	Chan and Zhang (1999)
Parameter estimate	Treatment difference
Point estimate	14.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.8
upper limit	57.9

Primary: Percentage of Subjects in Modified Clinical Remission at Week 12 (Modified Mayo Endoscopy Subscore = 0 or 1, Treatment Failure Approach)

End point title	Percentage of Subjects in Modified Clinical Remission at Week 12 (Modified Mayo Endoscopy Subscore = 0 or 1, Treatment Failure Approach)

End point description:

The Mayo score consists of 4 subscores (Endoscopic, stool frequency, rectal bleeding and Physician's global assessment [PGA]), each graded 0 to 3 with the higher score indicating more severe disease activity. Modified clinical remission is defined as a modified total Mayo Score (total Mayo score excluding the PGA subscore) with modified endoscopic subscore = 0 or 1 (where any friability was scored as a mayo endoscopic subscore of 2), stool frequency subscore = 0 or 1, and rectal bleeding subscore = 0. All subjects who had received at least one dose of the randomized treatment were included in the analysis population. Subjects with missing values were handled by treatment failure approach (subjects who had missing value for any reasons were considered as treatment failures).

End point type	Primary

End point timeframe:

Week 12

End point values	Placebo + Infliximab	PF-06687234 20 mg + Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Percentage of subjects (%)				
number (confidence interval 95%)	0 (0.0 to 26.7)	10 (0.5 to 44.4)		

Statistical analyses

Statistical analysis title	Treatment Difference Between 2 Arms
Comparison groups	Placebo + Infliximab v PF-06687234 20 mg + Infliximab

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5221
Method	Chan and Zhang (1999)
Parameter estimate	Treatment difference
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.7
upper limit	45.6

Primary: Number of Subjects with Treatment-Emergent Adverse Events (AEs; All Causalities)

End point title	Number of Subjects with Treatment-Emergent Adverse Events (AEs; All Causalities)[1]

End point description:

Treatment-emergent AEs are those with initial onset or that worsen in severity after the first dose of the study medication. An serious adverse event (SAE) is any untoward medical occurrence at any dose that: results in death; is life threatening (immediate risk of death); requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions); results in congenital anomaly/birth defect; or that is considered to be an important medical event that may jeopardize the subjects or may require intervention to prevent one of the other AE outcomes. Severe AEs were defined as AEs that interfered significantly with subjects's usual function. Both SAEs and severe AEs were according to the investigator's assessment. All subjects who had received at least one dose of the randomized treatment were included in the analysis population.

End point type	Primary

End point timeframe:

Baseline (Day 1) through and including a minimum of 28 calendar days after the last administration of the investigational products (22 weeks in total)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis were planned for safety endpoints.

End point values	Placebo + Infliximab	PF-06687234 20 mg + Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Subjects				
Subjects with AEs	8	9		
Subjects with SAEs	1	0		
Subjects with severe AEs	2	0		
Subjects discontinued from study due to AEs	0	0		
IP discontinued due to AEs, subjects continued	2	1		
Subjects with temporary discontinuation due to AEs	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Treatment-Emergent AEs (Treatment Related)

End point title	Number of Subjects with Treatment-Emergent AEs (Treatment Related)[2]

End point description:

Treatment-emergent AEs are those with initial onset or that worsen in severity after the first dose of the study medication. An SAE is any untoward medical occurrence at any dose that: results in death; is life threatening (immediate risk of death); requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions); results in congenital anomaly/birth defect; or that is considered to be an important medical event that may jeopardize the subjects or may require intervention to prevent one of the other AE outcomes. Severe AEs were defined as AEs that interfered significantly with subjects's usual function. Treatment-related AEs, SAEs and severe AEs were according to the investigator's assessment. All subjects who had received at least one dose of the randomized treatment were included in the analysis population.

End point type	Primary

End point timeframe:

Baseline (Day 1) through and including a minimum of 28 calendar days after the last administration of the investigational products (22 weeks in total)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis were planned for safety endpoints.

End point values	Placebo + Infliximab	PF-06687234 20 mg + Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Subjects				
Subjects with AEs	1	7		
Subjects with SAEs	0	0		
Subjects with severe AEs	0	0		
Subjects discontinued from study due to AEs	0	0		
IP discontinued due to AEs, subjects continued	1	0		
Subjects with temporary discontinuation due to AEs	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Laboratory Test Abnormalities Without Regard to

Baseline Abnormality

End point title	Number of Subjects with Laboratory Test Abnormalities Without Regard to Baseline Abnormality[3]

End point description:

The laboratory tests as defined in the protocol, including hematology, chemistry, urinalysis and other, were performed. Baseline was defined as the last measurement prior to first dosing (Day 1). All subjects with at least one observation of the given laboratory test while on study treatment or during lag time were included in the analysis population. LLN=lower limit of normal; ULN=upper limit of normal; LPF=low-power field; n=number of subjects with a laboratory abnormality meeting specified criteria while on study treatment or during lag time.

End point type	Primary

End point timeframe:

From baseline through Week 16

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis were planned for safety endpoints.

End point values	Placebo + Infliximab	PF-06687234 20 mg + Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Subjects				
Hemoglobin (g/dL) < 0.8 x LLN	0	2		
Hematocrit (%) < 0.8 x LLN	0	2		
Erythrocytes (10^6/mm^3) < 0.8 x LLN	0	2		
Reticulocytes (10^3/mm^3) > 1.5 x ULN	0	1		
Reticulocytes/Erythrocytes (%) > 1.5 x ULN	0	1		
Leukocytes (10^3/mm^3) > 1.5 x ULN	0	1		
Lymphocytes (10^3/mm^3) < 0.8 x LLN	2	2		
Lymphocytes/Leukocytes (%) < 0.8 x LLN	1	4		
Neutrophils (10^3/mm^3) < 0.8 x LLN	1	0		
Neutrophils (10^3/mm^3) > 1.2 x ULN	0	2		
Neutrophils/Leukocytes (%) < 0.8 x LLN	0	1		
Neutrophils/Leukocytes (%) > 1.2 x ULN	0	2		
Basophils/Leukocytes (%) > 1.2 x ULN	1	0		
Eosinophils (10^3/mm^3) > 1.2 x ULN	0	1		
Eosinophils/Leukocytes (%) > 1.2 x ULN	1	0		
Monocytes/Leukocytes (%) > 1.2 x ULN	2	2		
Protein (g/dL) < 0.8 x LLN	0	1		
Albumin (g/dL) < 0.8 x LLN	1	1		
Creatinine (mg/dL) > 1.3 x ULN	0	1		
Glucose (mg/dL) > 1.5 x ULN	0	1		
Ketones (Scalar) >=1	1	1		
Urine Protein (mg/dL) >=1	1	1		
Urine Hemoglobin (Scalar) >=1	3	3		
Leukocyte Esterase (Scalar) >=1	4	3		
Hyaline Casts (/LPF) > 1 (n=2, 2)	0	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Categorical Vital Signs

End point title	Number of Subjects With Categorical Vital Signs[4]

End point description:

Single sitting blood pressure (BP), pulse rate, and temperature were measured. At Day 1 and Week 1, BP and pulse were collected approximately 30 minutes prior to dosing, approximately 30 minutes post dosing and approximately 1 hour post dosing. For subjects with no safety issues (eg, severe injection site reactions, severe elevations BP and/or pulse), BP and pulse were collected approximately 30 minutes prior to dosing and approximately 30 minutes post dosing from Weeks 2-16. Vital signs were analyzed as per pre-specified categories. All subjects who had received at least one dose of the randomized treatment were included in the analysis population.

End point type	Primary

End point timeframe:

From baseline through Week 16

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis were planned for safety endpoints.

End point values	Placebo + Infliximab	PF-06687234 20 mg + Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Subjects				
Sitting systolic blood pressure (SBP) < 90 mmHg	0	0		
Increase in Sitting SBP >=30 mmHg	2	0		
Decrease in Sitting SBP >=30 mmHg	0	0		
Sitting diastolic blood pressure (DBP) < 50 mmHg	0	0		
Increase in Sitting DBP >=20 mmHg	2	2		
Decrease in Sitting DBP >=20 mmHg	3	2		
Sitting Pulse Rate < 40 beats/minute	0	0		
Sitting Pulse Rate > 120 beats/minute	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Categorical Electrocardiogram (ECG) data

End point title	Number of Subjects With Categorical Electrocardiogram (ECG) data[5]

End point description:

Twelve (12) lead ECGs were collected. All scheduled ECGs were performed after the subjects had rested quietly for at least 10 minutes in a supine position. When the timing of these measurements coincided with a blood collection, the ECG was obtained prior to the nominal time of the blood collection, blood pressure, and pulse rate. ECG data were analyzed as per pre-specified categories. All subjects who had received at least one dose of the randomized treatment were included in the analysis population.
PR=pulse rate; QTc=QT interval corrected for heart rate; QTcF=QTc corrected using Fridericia's formula.

End point type	Primary

End point timeframe:

From baseline through Week 16

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis were planned for safety endpoints.

End point values	Placebo + Infliximab	PF-06687234 20 mg + Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Subjects				
PR Interval >=300 millisecond (msec)	0	0		
Change in PR Interval (%) >=25/50%	0	0		
QRS Complex >=140 msec	0	0		
Change in QRS Complex (%) >=50%	0	0		
QT Interval >=500 msec	0	0		
450 msec <= QTcF < 480 msec	0	0		
480 msec <= QTcF < 500 msec	0	0		
QTcF >=500 msec	0	0		
30 msec <= change in QTcF < 60 msec	0	1		
Change in QTcF >= 60 msec	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Endoscopic Improvement at Week 12 (Observed Cases)

End point title	Percentage of Subjects With Endoscopic Improvement at Week 12 (Observed Cases)

End point description:

Endoscopic improvement is defined as a decrease of >=1 point in a modified endoscopic subscore or an absolute endoscopy score of <=1 without friability. All subjects who had received at least one dose of the randomized treatment were included in the analysis population. Subjects with missing values were handled by observed case approach (the missing data were used as is). The number of subjects with observed data were 8 for the Placebo + Infliximab arm and 7 for PF-06687234 20 mg + Infliximab arm. The percentage of subjects achieving endoscopic improvement was calculated based on the number of subjects with observed data.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo + Infliximab	PF-06687234 20 mg + Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Percentage of subjects (%)				
number (confidence interval 95%)	25.0 (4.6 to 65.1)	57.1 (22.5 to 87.1)		

Statistical analyses

Statistical analysis title	Treatment Difference Between 2 Arms
Comparison groups	Placebo + Infliximab v PF-06687234 20 mg + Infliximab
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3166
Method	Chan and Zhang (1999)
Parameter estimate	Treatment difference
Point estimate	32.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.7
upper limit	74.1

Secondary: Percentage of Subjects With Endoscopic Improvement at Week 12 (Treatment Failure Approach)

End point title	Percentage of Subjects With Endoscopic Improvement at Week 12 (Treatment Failure Approach)

End point description:

Endoscopic improvement is defined as a decrease of >=1 point in a modified endoscopic subscore or an absolute endoscopy score of <=1 without friability. Subjects with missing values were handled by treatment failure approach (subjects who had missing value for any reasons were considered as treatment failures). All subjects who had received at least one dose of the randomized treatment were included in the analysis population.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo + Infliximab	PF-06687234 20 mg + Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Percentage of subjects (%)				
number (confidence interval 95%)	20.0 (3.7 to 55.6)	40.0 (15.0 to 73.3)		

Statistical analyses

Statistical analysis title	Treatment Difference Between 2 Arms
Comparison groups	Placebo + Infliximab v PF-06687234 20 mg + Infliximab
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5234
Method	Chan and Zhang (1999)
Parameter estimate	Treatment difference
Point estimate	20
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.9
upper limit	58.5

Secondary: Change from Baseline in Geboes Ulcerative Colitis Score at Week 12 (Baseline Observation Carried Forward [BOCF])

End point title	Change from Baseline in Geboes Ulcerative Colitis Score at Week 12 (Baseline Observation Carried Forward [BOCF])

End point description:

Geboes scores is a structured six-grade classification system ordered as follows: 0, structural changes; 1, chronic inflammatory infiltrate; 2, lamina propria neutrophils and eosinophils; 3, neutrophils in epithelium; 4, crypt destruction; and 5, erosion and ulceration. Robart's histology scores is based on the Geboes scores, and the final score is obtained by combining the sub-scores of four main items (chronic inflammatory infiltrate level, lamina propria neutrophils, neutrophils in the epithelium, and erosion or ulceration), which are classified from 0 to 3, yielding a final score that ranges between 0 and 5.4. The BOCF approach was used to handle the monotone missing data or no post baseline measurements. The baseline values were carried forward for the visits after which subjects prematurely discontinued assigned treatment. All subjects who had received at least one dose of the randomized treatment were included in the analysis population.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo + Infliximab	PF-06687234 20 mg + Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Scores on a scale				
least squares mean (confidence interval 95%)	-10.08 (-16.95 to -3.20)	-6.02 (-12.90 to 0.85)		

Statistical analyses

Statistical analysis title	Treatment Difference Between 2 Arms
Comparison groups	Placebo + Infliximab v PF-06687234 20 mg + Infliximab
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3928
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	4.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	13.8

Secondary: Change from Baseline in Robart's Histology Index at Week 12 (Observed Cases)

End point title	Change from Baseline in Robart's Histology Index at Week 12 (Observed Cases)

End point description:

Robart’s histology scores is based on the Geboes scores, and the final score is obtained by combining the sub-scores of four main items (chronic inflammatory infiltrate level, lamina propria neutrophils, neutrophils in the epithelium, and erosion or ulceration), which are classified from 0 to 3, yielding a final score that ranges between 0 and 33. All subjects who had received at least one dose of the randomized treatment were included in the analysis population. Subjects with missing values were handled by observed case approach (the missing data were used as is). The number of subjects with observed data at Week 12 were 8 each for the Placebo + Infliximab arm and PF-06687234 20mg + Infliximab arm.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo + Infliximab	PF-06687234 20 mg + Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: Scores on a scale				
least squares mean (confidence interval 95%)	-12.96 (-20.60 to -5.32)	-7.16 (-14.81 to 0.48)		

Statistical analyses

Statistical analysis title	Treatment Difference Between 2 Arms
Comparison groups	Placebo + Infliximab v PF-06687234 20 mg + Infliximab
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2705
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	5.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.08
upper limit	16.67

Secondary: Percentage of Subjects With a Clinical Response at Week 12 (Observed Cases)

End point title	Percentage of Subjects With a Clinical Response at Week 12 (Observed Cases)

End point description:

Clinical response is defined with a decrease from baseline of at least 3 points in total Mayo score with at least 30% change, accompanied by at least one-point decrease or absolute score of 0 or 1 in rectal bleeding subscore. All subjects who had received at least one dose of the randomized treatment were included in the analysis population. Subjects with missing values were handled by observed case approach (the missing data were used as is). The number of subjects with observed data were 8 for the Placebo + Infliximab arm and 7 for PF-06687234 20mg + Infliximab arm. The percentage of subjects achieving clinical response was calculated based on the number of subjects analyzed.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo + Infliximab	PF-06687234 20 mg + Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Percentage of subjects (%)				
number (confidence interval 95%)	37.5 (11.1 to 71.1)	85.7 (44.6 to 99.3)		

Statistical analyses

Statistical analysis title	Treatment Difference Between 2 Arms
Comparison groups	Placebo + Infliximab v PF-06687234 20 mg + Infliximab
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0732
Method	Chan and Zhang (1999)
Parameter estimate	Treatment difference
Point estimate	48.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.4
upper limit	84.7

Secondary: Percentage of Subjects With a Clinical Response at Week 12 (Treatment Failure Approach)

End point title	Percentage of Subjects With a Clinical Response at Week 12 (Treatment Failure Approach)

End point description:

Clinical response is defined with a decrease from baseline of at least 3 points in total Mayo score with at least 30% change, accompanied by at least one-point decrease or absolute score of 0 or 1 in rectal bleeding subscore. All subjects who had received at least one dose of the randomized treatment were included in the analysis population. Subjects with missing values were handled by treatment failure approach (subjects who had missing value for any reasons were considered as treatment failures).

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo + Infliximab	PF-06687234 20 mg + Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Percentage of subjects (%)				
number (confidence interval 95%)	30.0 (8.7 to	60.0 (26.7 to		

61.9)	85.0)

Statistical analyses

Statistical analysis title	Treatment Difference Between 2 Arms
Comparison groups	Placebo + Infliximab v PF-06687234 20 mg + Infliximab
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2633
Method	Chan and Zhang (1999)
Parameter estimate	Treatment difference
Point estimate	30
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.4
upper limit	69.2

Secondary: Percentage of Subjects With Change From Baseline in Derived Partial Mayo Score of <=2 With no Individual Subscore >1 at Weeks 2, 4, 8 and 12 (Observed Cases)

End point title	Percentage of Subjects With Change From Baseline in Derived Partial Mayo Score of <=2 With no Individual Subscore >1 at Weeks 2, 4, 8 and 12 (Observed Cases)

End point description:

Derived partial mayo score is defined as total mayo score excluding the endoscopic subscore (stool frequency, rectal bleeding and physician's global assessment only), ranging from 0 to 9. All subjects who had received at least one dose of the randomized treatment were included in the analysis population. Subjects with missing values were handled by observed case approach (the missing data were used as is). Generalized Linear Mixed Model (GLMM) was used with fixed effects of treatment, visit and treatment by visit interaction. n=number of subjects with change from baseline.

End point type	Secondary

End point timeframe:

Baseline, weeks 2, 4, 8 and 12

End point values	Placebo + Infliximab	PF-06687234 20 mg + Infliximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Percentage of subjects (%)				
number (confidence interval 95%)				
Week 2 (n=10, 10)	50.0 (21.0 to 79.0)	50.0 (21.0 to 79.0)		

Week 4 (n=10, 10)	50.0 (21.0 to 79.0)	60.0 (27.9 to 85.3)		
Week 8 (n=9, 9)	62.5 (28.9 to 87.2)	50.8 (20.9 to 80.1)		
Week 12 (n=8, 7)	64.9 (29.8 to 89.0)	64.8 (28.6 to 89.4)		

Statistical analyses

Statistical analysis title	Treatment Difference Between 2 Arms
Statistical analysis description:	
At Week 2	
Comparison groups	Placebo + Infliximab v PF-06687234 20 mg + Infliximab
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Generalized Linear Mixed Model
Parameter estimate	Odds ratio (OR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.15
upper limit	6.54

Statistical analysis title	Treatment Difference Between 2 Arms
Statistical analysis description:	
At Week 4	
Comparison groups	Placebo + Infliximab v PF-06687234 20 mg + Infliximab
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6691
Method	Generalized Linear Mixed Model
Parameter estimate	Odds ratio (OR)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	10

Statistical analysis title	Treatment Difference Between 2 Arms

Statistical analysis description:	
At Week 8	
Comparison groups	Placebo + Infliximab v PF-06687234 20 mg + Infliximab
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6248
Method	Generalized Linear Mixed Model
Parameter estimate	Odds ratio (OR)
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	4.4

Statistical analysis title	Treatment Difference Between 2 Arms
Statistical analysis description:	
At Week 12	
Comparison groups	Placebo + Infliximab v PF-06687234 20 mg + Infliximab
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9965
Method	Generalized Linear Mixed Model
Parameter estimate	Odds ratio (OR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	8.3

Secondary: Serum concentrations of PF-06687234 20 mg

End point title	Serum concentrations of PF-06687234 20 mg[6]

End point description:

Samples for serum PF-06687234 concentration were collected at timepoints defined by the protocol. Concentration values below the lower limit of quantification were excluded when calculating the geometric mean (geometric coefficient of variation). All subjects who received at least one dose of PF-06687234, had data on at least one PK concentration (above or equal to lower limit of quantification) and did not participate in PK substudy were included in the analysis. NALQ=number of subjects with observations above or equal to lower limit of quantification. There were no subjects with qualified data for the analysis on Day 1, at Weeks 1 and 16, hence the results were entered as 99999 (not available).

End point type	Secondary

End point timeframe:

Prior to dosing on Day 1, at Weeks 1, 3, 7, 11, 12 (168 hours post dose) and 16

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The PK data reporting is not applicable for the placebo arm.

End point values	PF-06687234 20 mg + Infliximab			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: nanogram/milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Day 1 (NALQ=0)	99999 (± 99999)			
Week 1 (NALQ=0)	99999 (± 99999)			
Week 3 (NALQ=2)	0.4537 (± 42)			
Week 7 (NALQ=6)	0.4494 (± 27)			
Week 11 (NALQ=3)	0.4713 (± 2)			
Week 12 (NALQ=3)	0.5140 (± 40)			
Week 16 (NALQ=0)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With the Development of Human Anti-Fusion Antibodies (HAFAs) and Neutralizing Antibodies (NAbs) Against PF-06687234

End point title	Percentage of Subjects With the Development of Human Anti-Fusion Antibodies (HAFAs) and Neutralizing Antibodies (NAbs) Against PF-06687234[7]

End point description:

Plasma samples were analyzed for anti PF-06687234, anti PF-06687234 Interleukin-10 (IL-10) NAb and anti PF-06687234 single chain variable fragment (scFv) NAb. Samples inadvertently analyzed were excluded. All subjects who received at least one dose of PF-06687234 and with at least one post treatment HAFA determination were included in the analysis population. N=number of subjects with observed data. The percentages of subjects with the development of HAFAs and NAbs against PF-06687234 were calculated based on the number of subjects with observed data.

End point type	Secondary

End point timeframe:

At screening, Day 1, Weeks 3, 7, 11, 12 and 16 (prior to dosing)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The percentage of subjects with the development of HAFAs and NAbs against PF-06687234 did not apply to the placebo arm.

End point values	PF-06687234 20 mg + Infliximab			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Percentage of subjects (%)				
number (not applicable)				
Anti PF-06687234 (Screening; N=10)	0			
Anti PF-06687234 (Day 1; N=10)	10.0			
Anti PF-06687234 (Week 3; N=10)	30.0			
Anti PF-06687234 (Week 7; N=8)	50.0			
Anti PF-06687234 (Week 11; N=7)	28.6			
Anti PF-06687234 (Week 12; N=7)	28.6			
Anti PF-06687234 (Week 16; N=8)	12.5			
Anti PF-06687234 IL-10 NAb (Screening; N=0)	0			
Anti PF-06687234 IL-10 NAb (Day 1; N=1)	0			
Anti PF-06687234 IL-10 NAb (Week 3; N=3)	0			
Anti PF-06687234 IL-10 NAb (Week 7; N=4)	0			
Anti PF-06687234 IL-10 NAb (Week 11; N=2)	0			
Anti PF-06687234 IL-10 NAb (Week 12; N=2)	0			
Anti PF-06687234 IL-10 NAb (Week 16; N=1)	0			
Anti PF-06687234 scFv NAb (Screening; N=0)	0			
Anti PF-06687234 scFv NAb (Day 1; N=1)	0			
Anti PF-06687234 scFv NAb (Week 3; N=3)	0			
Anti PF-06687234 scFv NAb (Week 7; N=4)	50.0			
Anti PF-06687234 scFv NAb (Week 11; N=2)	0			
Anti PF-06687234 scFv NAb (Week 12; N=2)	0			
Anti PF-06687234 scFv NAb (Week 16; N=1)	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time the subject provided informed consent through approximately Week 26. For subjects who were screen failures, the active collection period ended when screen failure status was determined.

Adverse event reporting additional description:

All 20 subjects were included in the analysis for AEs and SAEs.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Placebo + Infliximab

Reporting group description:

Placebo for PF06687234 was administered as subcutaneous injection on Day 1, Week 1 (Day 8), Week 2 (Day 15), Week 3 (Day 22), Week 4 (Day 29), Week 5 (Day 36), Week 6 (Day 43), Week 7 (Day 50), Week 8 (Day 57), Week 9 (Day 64), Week 10 (Day 71) and Week 11 (Day 78) for a total 12 doses. Remicade or protocol specified infliximab biosimilar was administered as an IV infusion on Day 1, Week 8 and Week 16 for a total of 3 doses for subjects on infliximab every 8 weeks, and Day 1, Week 6, Week 12 and Week 18 for subjects on infliximab every 6 weeks.

Reporting group title	PF-06687234 20 mg + Infliximab

Reporting group description:

PF-06687234 was administered as a 20 mg subcutaneous injection on Day 1, Week 1 (Day 8), Week 2 (Day 15), Week 3 (Day 22), Week 4 (Day 29), Week 5 (Day 36), Week 6 (Day 43), Week 7 (Day 50), Week 8 (Day 57), Week 9 (Day 64), Week 10 (Day 71) and Week 11 (Day 78) for a total 12 doses. Remicade or protocol specified infliximab biosimilar was administered as an IV infusion on Day 1, Week 8 and Week 16 for a total of 3 doses for subjects on infliximab every 8 weeks, and Day 1, Week 6, Week 12 and Week 18 for subjects on infliximab every 6 weeks.

Serious adverse events	Placebo + Infliximab	PF-06687234 20 mg + Infliximab	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo + Infliximab	PF-06687234 20 mg + Infliximab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 10 (70.00%)	9 / 10 (90.00%)	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	
Fatigue			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	6	
Injection site reaction			
subjects affected / exposed	0 / 10 (0.00%)	3 / 10 (30.00%)	
occurrences (all)	0	7	
Injection site erythema			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Oedema			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Xerosis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Injection site rash			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Vulvovaginal discomfort			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			

Stress			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Investigations			
Cardiac murmur			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	2 / 10 (20.00%)	2 / 10 (20.00%)	
occurrences (all)	2	3	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Abdominal pain lower			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Colitis ulcerative			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Gastritis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	

Proctalgia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Glossitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Diabetic nephropathy			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Micturition urgency			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Onychomycosis			

subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Tooth infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	
occurrences (all)	1	3	
Metabolism and nutrition disorders			
Vitamin B12 deficiency			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 September 2017	1. Throughout the protocol modified language to allow the use of specific infliximab biosimilars; 2. Added Appendix 5 Protocol Specific Infliximab Biosimilars; 3. Changed the collection of the serum infliximab concentration and ADA against infliximab from Visit 8 Week 7 to Visit 9 Week 8; 4. Modified inclusion criterion #7 to provide further clarification regarding the infliximab treatment regimen that is required at study entry and throughout the study; 5. Modified exclusion criteria #24 hemoglobin level from <=95 g/L (9.5 g/dL) to <=100 g/L (10.0 g/dL); 6. Modified Prohibited Medications to further clarify and cover the timeframe that iTNF treatment or biologic therapy other than infliximab iTNF treatment that would be prohibited during the study, and to correct typographical error and duplicative language; 7. Modified the collection time for Plasma PF06687234 concentration sample at Week 12/Early Withdrawal Visit; 8. Removed automatic hemoglobin retesting criteria to limit the number of blood draws and leave it up to discretion of investigator regarding retesting necessity and timing; 9. Provided additional guidance to regulators and investigators on individual subject discontinuation criteria for specific AST or ALT results when co-occurring with specific symptoms; 10. Added the following specific language in Section 6.4 to further protect patient safety and to establish requirement for prompt adhoc IRC review meetings in setting where a severe AE or an SAE is assessed as potentially causally related to the investigational product have been met and the required notification to relevant regulatory authorities regarding the adhoc IRC meeting and relevant case details; 11. Added Reference: Schroeder KW, Tremaine WJ and Listrup DM. NEJM 1987;24;317(26) 1625-1629.
06 March 2018	Updated enrollment and safety information in Philogen Dekavil RA study; 2. Deleted "or legally acceptable representative" in Criterion #1 and in Sections 8.1.2 and 12.3; 3. Modified the inclusion criterion #3 to add "weight >40 kg"; 4. Added exclusion criterion #30 to exclude subjects who had known history of hypersensitivity, intolerance or allergic reaction to IP or any constituent of the IP; 5. Updated the exclusion criterion #18 to protect safety of the study subjects and comply with regulatory request; 6. Section 4.4.1 Contraception: Removed 'using male or female condom plus spermicide as a highly effective method of contraception' and modified the contraception requirement to '2 methods of contraception (at least one of which is considered to be highly effective)'; 7. Section 4.4.1 Contraception: Added "Male subjects must refrain from sperm donation for the duration of the active treatment period and until Week 16 or 28 days after the last dose of the investigational product.; 8. Added a new subsection 5.11 Rescue Medication to provide clarification that rescue therapy should be provided by investigators as deemed clinically appropriate and that subjects requiring rescue medication will be discontinued from the study; 9. Clarified in the Section 5.2 Breaking the Blind that if the immediate unblinding is necessary, the discussion between investigator and the member of study team member is not required in advance of unblinding; 10. Clarified that IP and placebo are prepared by qualified unblinded site staff and administration of prepared IP or placebo to subjects is performed by qualified blinded site staff; 11. Added a discontinuation criterion that a subject with detected neutralizing antibody against IL10 domain will be discontinued from the treatment and the study; 12. Replaced the reference #22 with "Chan ISF., Zhang Z. Test-based exact confidence intervals for the difference of two binomial proportions. Biometrics, 1999; 55: 1201–1209."

30 August 2018	Safety related: 1.Added text for subject discontinuation in the presence of detectable NAb against IL10 portion of PF06687432 in Schedule of Activities; 2. Widened the interval between infliximab infusion completion and IP dosing; 3. Provided rationale, references, and practice guidance to allow infliximab dosing every 6 weeks in the protocol; 4. Changed to allow subjects on infliximab dosing interval of every 6 weeks into the study and clarified the time requirement for study eligibility after change of infliximab regimen (dosage and dosing interval); 5. Modified the criterion to state "Subjects who have partial response to antiTNF (infliximab) and active UC as defined by (via screening endoscopy) a total Mayo Score >=4 but <=9 and an endoscopic subscore >=2; 6. Modified inclusion criterion #6 to allow the inclusion of subjects with disease severity consistent with other inclusion criteria whilst still excluding subjects with isolated proctitis; 7. Modified exclusion criterion 4 to clarify that a colonoscopy is required for subjects with extensive colitis and without surveillance colonoscopy within 2 years and that this surveillance can be performed during the screening colonoscopy if necessary; 8. Clarified the exclusion criterion #5 that subjects with prior history of adenomatous polyps will be eligible if the polyps have been completely removed and pathology is negative; 9. Section 4.2, exclusion criterion#24: Changed the exclusion criterion eGFR to <60 mL/min/1.73 mm^2 based on age appropriate calculation; 10. Revised exclusion criterion is to exclude subjects with evidence of active TB or latent TB patients without adequate treatment into the study; 11. Updated with newly available 6 months toxicity data in mice and revised the safety margin based on clinical dose of 0.5 mg/kg/week.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported