Clinical trial results:
A Double-Blind, Randomized, Placebo-Controlled, Dose Ranging Study to Evaluate the Efficacy and Safety of PF-04236921 in Subjects With Crohn's Disease Who are Anti-TNF Inadequate Responders (ANDANTE)

Summary

EudraCT number	2010-023034-23
Trial protocol	IE HU GB GR DK DE BE IT CZ AT SE
Global end of trial date	26 February 2015

Results information

Result version number	v1 (current)
This version publication date	10 March 2016
First version publication date	10 March 2016

Trial information

Trial identification

Sponsor protocol code	B0151003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01287897
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc
Sponsor organisation address	235 E 42nd Street, New York, United States, 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer ClinicalTrials.gov Call Center, 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer ClinicalTrials.gov Call Center, 001 8007181021, 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	15 July 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 February 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to demonstrate clinical activity of PF 04236921 that would induce a clinical response and remission in subjects with CD via the CDAI and to select dose(s) for future clinical studies.

Protection of trial subjects:

A signed and dated informed consent was required before any protocol specific screening procedures were performed. The investigators explained the nature, purpose, and risks of the study to each subject. Each subject was informed that he/she could withdraw from the study at any time and for any reason. Each subject was given sufficient time to consider the implications of the study before deciding whether to participate. Subjects who chose to participate signed an informed consent document. An external independent data monitoring committee (DMC) consisting of external DMC physicians and statistician were established to review the safety of subjects on an ongoing basis including adverse event of special interest and to adjudicate any cases of abdominal or perineal abscess that occurred during the study

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 February 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research, Safety
Long term follow-up duration	7 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 7
Country: Number of subjects enrolled	Brazil: 9
Country: Number of subjects enrolled	Canada: 18
Country: Number of subjects enrolled	Israel: 13
Country: Number of subjects enrolled	New Zealand: 5
Country: Number of subjects enrolled	Switzerland: 7
Country: Number of subjects enrolled	United States: 80
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Belgium: 17
Country: Number of subjects enrolled	Czech Republic: 9
Country: Number of subjects enrolled	Denmark: 14
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 17

Country: Number of subjects enrolled	Hungary: 9
Country: Number of subjects enrolled	Ireland: 6
Country: Number of subjects enrolled	Italy: 23
Worldwide total number of subjects	247
EEA total number of subjects	108

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)	240
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study included a 28-day screening period, an induction period (Week 0-12) and a 28-week follow-up period. Subjects who completed the induction treatment period could enter the follow-up period or an open-label extension study, B0151005. Subjects who discontinued treatment during the induction period could enter the follow-up period.

Pre-assignment

Screening details:

A total of 250 subjects were randomized via Interactive Voice Response System (IVRS); of which, 247 received investigational product and 3 were randomized inadvertently and not dosed (2 did not meet entrance criteria and 1 did not consent properly and was not included in clinical database because the randomization page was not completed).

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, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The subjects, investigators, site personnel and sponsor personnel/designee who interacted with the investigators were blinded throughout the study (while others unblinded during follow up). An independent unblinded team performed the interim analysis.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo administered subcutaneously (SC) in the anterolateral right and left thighs on Day 1 and Day 28. Each subject received 2 injections due to the double-dummy design of the study.

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

Dosage and administration details:

Placebo 0 mg was administered on Day 1 and Day 28

Arm title	PF-04236921 10 milligram (mg)

Arm description:

PF-04236921 10 mg administered SC in the anterolateral right and left thighs on Day 1 and Day 28. Each subject received 2 injections due to the double-dummy design of the study.

Arm type	Experimental
Investigational medicinal product name	PF-04236921
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

PF-04236921 10 mg was administered subcutaneously (SC) on Day 1 and Day 28

Arm title	PF-04236921 50 mg

Arm description:

PF-04236921 50 mg administered SC in the anterolateral right and left thighs on Day 1 and Day 28. Each subject received 2 injections due to the double-dummy design of the study.

Arm type	Experimental
Investigational medicinal product name	PF-04236921
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

PF-04236921 50 mg was administered on Day 1 and Day 28

Arm title	PF-04236921 200 mg

Arm description:

PF-04236921 200 mg administered SC in the anterolateral right and left thighs on Day 1 and Day 28. Each subject received 2 injections due to the double-dummy design of the study.

Arm type	Experimental
Investigational medicinal product name	PF-04236921
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

PF-04236921 200 mg was administered on Day 1 and Day 28

Number of subjects in period 1	Placebo	PF-04236921 10 milligram (mg)	PF-04236921 50 mg
Started	69	67	71
Treated	69	67	71
Completed treatment period	58 [1]	52 [2]	58 [3]
Completed follow-up period	3 [4]	8 [5]	3 [6]
Enrolled in B0151005	56 [7]	50 [8]	56 [9]
Completed	59	58	59
Not completed	10	9	12
Consent withdrawn by subject	1	5	3
Adverse event, non-fatal	5	3	6
Unspecified	1	-	1
Lost to follow-up	-	-	2
Lack of efficacy	2	-	-
Protocol deviation	1	1	-

Number of subjects in period 1	PF-04236921 200 mg
Started	40
Treated	40
Completed treatment period	29 [10]

Completed follow-up period	4 [11]
Enrolled in B0151005	29 [12]
Completed	33
Not completed	7
Consent withdrawn by subject	2
Adverse event, non-fatal	4
Unspecified	-
Lost to follow-up	-
Lack of efficacy	-
Protocol deviation	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The number of subjects under "completed" and "not completed" adds up to the number under "treated". The categories of "completed treatment period", "completed follow-up period" and "enrolled in B0151005" are NOT mutually exclusive as some subjects are counted in more than 1 of these.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The number of subjects under "completed" and "not completed" adds up to the number under "treated". The categories of "completed treatment period", "completed follow-up period" and "enrolled in B0151005" are NOT mutually exclusive as some subjects are counted in more than 1 of these.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The number of subjects under "completed" and "not completed" adds up to the number under "treated". The categories of "completed treatment period", "completed follow-up period" and "enrolled in B0151005" are NOT mutually exclusive as some subjects are counted in more than 1 of these.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The number of subjects under "completed" and "not completed" adds up to the number under "treated". The categories of "completed treatment period", "completed follow-up period", and "enrolled in B0151005" are NOT mutually exclusive as some subjects are counted in more than 1 of these.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The number of subjects under "completed" and "not completed" adds up to the number under "treated". The categories of "completed treatment period", "completed follow-up period", and "enrolled in B0151005" are NOT mutually exclusive as some subjects are counted in more than 1 of these.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The number of subjects under "completed" and "not completed" adds up to the number under "treated". The categories of "completed treatment period", "completed follow-up period", and "enrolled in B0151005" are NOT mutually exclusive as some subjects are counted in more than 1 of these.

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The number of subjects under "completed" and "not completed" adds up to the number under "treated". The categories of "completed treatment period", "completed follow-up period" and "enrolled in B0151005" are NOT mutually exclusive as some subjects are counted in more than 1 of these.

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The number of subjects under "completed" and "not completed" adds up to the number under "treated". The categories of "completed treatment period", "completed follow-up period" and "enrolled in B0151005" are NOT mutually exclusive as some subjects are counted in more than 1 of these.
[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The number of subjects under "completed" and "not completed" adds up to the number under "treated". The categories of "completed treatment period", "completed follow-up period" and "enrolled in B0151005" are NOT mutually exclusive as some subjects are counted in more than 1 of these.
[10] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The number of subjects under "completed" and "not completed" adds up to the number under "treated". The categories of "completed treatment period", "completed follow-up period" and "enrolled in B0151005" are NOT mutually exclusive as some subjects are counted in more than 1 of these.
[11] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The number of subjects under "completed" and "not completed" adds up to the number under "treated". The categories of "completed treatment period", "completed follow-up period", and "enrolled in B0151005" are NOT mutually exclusive as some subjects are counted in more than 1 of these.
[12] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The number of subjects under "completed" and "not completed" adds up to the number under "treated". The categories of "completed treatment period", "completed follow-up period" and "enrolled in B0151005" are NOT mutually exclusive as some subjects are counted in more than 1 of these.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo administered subcutaneously (SC) in the anterolateral right and left thighs on Day 1 and Day 28. Each subject received 2 injections due to the double-dummy design of the study.	
Reporting group title	PF-04236921 10 milligram (mg)
Reporting group description:	
PF-04236921 10 mg administered SC in the anterolateral right and left thighs on Day 1 and Day 28. Each subject received 2 injections due to the double-dummy design of the study.	
Reporting group title	PF-04236921 50 mg
Reporting group description:	
PF-04236921 50 mg administered SC in the anterolateral right and left thighs on Day 1 and Day 28. Each subject received 2 injections due to the double-dummy design of the study.	
Reporting group title	PF-04236921 200 mg
Reporting group description:	
PF-04236921 200 mg administered SC in the anterolateral right and left thighs on Day 1 and Day 28. Each subject received 2 injections due to the double-dummy design of the study.	

Reporting group values	Placebo	PF-04236921 10 milligram (mg)	PF-04236921 50 mg
Number of subjects	69	67	71
Age categorical Units: Subjects			
Adults (18-64 years)	68	66	69
From 65-84 years	1	1	2
Age Continuous | Units: Years			
arithmetic mean	38.4	38.9	38.9
standard deviation	± 13.6	± 12.9	± 13.1
Gender, Male/Female Units: Participants			
Female	38	34	44
Male	31	33	27

Reporting group values	PF-04236921 200 mg	Total	
Number of subjects	40	247	
Age categorical Units: Subjects			
Adults (18-64 years)	37	240	
From 65-84 years	3	7	
Age Continuous | Units: Years			
arithmetic mean	42.2		
standard deviation	± 13.2	-	
Gender, Male/Female Units: Participants			
Female	25	141	
Male	15	106	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo administered subcutaneously (SC) in the anterolateral right and left thighs on Day 1 and Day 28. Each subject received 2 injections due to the double-dummy design of the study.	
Reporting group title	PF-04236921 10 milligram (mg)
Reporting group description:	
PF-04236921 10 mg administered SC in the anterolateral right and left thighs on Day 1 and Day 28. Each subject received 2 injections due to the double-dummy design of the study.	
Reporting group title	PF-04236921 50 mg
Reporting group description:	
PF-04236921 50 mg administered SC in the anterolateral right and left thighs on Day 1 and Day 28. Each subject received 2 injections due to the double-dummy design of the study.	
Reporting group title	PF-04236921 200 mg
Reporting group description:	
PF-04236921 200 mg administered SC in the anterolateral right and left thighs on Day 1 and Day 28. Each subject received 2 injections due to the double-dummy design of the study.	

Primary: The CDAI-70 response rate at Week 8 in subjects who received placebo, PF-04236921 10 mg and PF-04236921 50 mg

End point title	The CDAI-70 response rate at Week 8 in subjects who received placebo, PF-04236921 10 mg and PF-04236921 50 mg[1]
End point description:	
Crohn’s Disease Activity Index (CDAI)-70 response was defined as a decrease in CDAI score of 70 or greater from baseline. The proportions of subjects with CDAI-70 response at Week 8 were compared between placebo and PF-04236921 10 mg/50 mg. CDAI is used to quantify the symptoms of patients with Crohn's Disease. CDAI evaluates 8 Crohn's disease-related variables during a 1-week assessment period, yielding a composite score greater than or equal to (>=) 0 and without an upper limit. Many clinical trials use the endpoint for response as a 70 or greater point decrease in CDAI and clinical remission is often defined as a CDAI score below 150. Primary analysis: full analysis set (FAS, defined as all randomized subjects who received at least 1 dose of study treatment; 2 subjects [10 mg arm] excluded due to a quality issue) excluding 200 mg (halted prematurely before reaching the planned sample size and thus no longer powered at the planned level to test against placebo).	
End point type	Primary
End point timeframe:	
Baseline and Week 8	
Notes:	
[1] - 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: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.	

End point values	Placebo	PF-04236921 10 milligram (mg)	PF-04236921 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	65	71	
Units: percentage of subjects				
least squares mean (confidence interval 90%)	30.6 (18.7 to 45.9)	35 (21.6 to 51.1)	49.3 (34.1 to 64.7)	

Statistical analyses

Statistical analysis title	Comparison between 10 mg and placebo at Week 8

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.3406 [3]
Method	Generalized linear mixed model (GLMM)
Parameter estimate	Mean difference (final values)
Point estimate	4.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-13
upper limit	21.7
Variability estimate	Standard error of the mean
Dispersion value	10.5

Notes:

[2] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

[3] - Type I rate was controlled for the 2 time points (Week 8 and Week 12) at 0.05 (one sided).

Statistical analysis title	Comparison between 50 mg and placebo at Week 8

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.0438 [5]
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	18.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.7
upper limit	36.7
Variability estimate	Standard error of the mean
Dispersion value	11

Notes:

[4] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.
[5] - Type I rate was controlled for the 2 time points (Week 8 and Week 12) at 0.05 (one sided).

Primary: The CDAI-70 response rate at Week 8 in subjects who received placebo and PF-04236921 200 mg

End point title	The CDAI-70 response rate at Week 8 in subjects who received placebo and PF-04236921 200 mg[6]

End point description:

CDAI-70 response was defined as a decrease in CDAI score of 70 or greater from baseline. The proportions of subjects with CDAI-70 response at Week 8 were compared between placebo and PF-04236921 200 mg. CDAI is used to quantify the symptoms of patients with Crohn's Disease. CDAI evaluates 8 Crohn's disease-related variables during a 1-week assessment period, yielding a composite score >=0 and without an upper limit. Many clinical trials use the endpoint for response as a 70 or greater point decrease in CDAI and clinical remission is often defined as a CDAI score below 150. The analysis was performed on FAS subjects of the 200 mg and placebo arms, referred to as FAS 200 mg versus (vs) placebo. The 200 mg arm was halted before reaching the planned sample size of approximately 60 and was no longer powered at the planned level to test against placebo. Thus, the 200 mg vs placebo comparison is a sensitivity analysis.

End point type	Primary

End point timeframe:

Baseline and Week 8

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: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	Placebo	PF-04236921 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	29		
Units: percentage of subjects				
least squares mean (confidence interval 90%)	28.8 (15.4 to 47.4)	39 (19.3 to 63.1)		

Statistical analyses

Statistical analysis title	Comparison between 200 mg and placebo at Week 8

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference). Since the inputs in the model included different Analysis Population than in End Point 1, that will yield different estimates for placebo for the two different models.

Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 0.2258 [8]
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	10.2

Confidence interval	
level	90 %
sides	2-sided
lower limit	-12.1
upper limit	32.6
Variability estimate	Standard error of the mean
Dispersion value	13.6

Notes:

[7] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.
[8] - Type I rate was controlled for the 2 time points (Week 8 and Week 12) at 0.05 (one sided).

Primary: The CDAI-70 response rate at Week 12 in subjects who received placebo, PF-04236921 10 mg and PF-04236921 50 mg

End point title	The CDAI-70 response rate at Week 12 in subjects who received placebo, PF-04236921 10 mg and PF-04236921 50 mg[9]

End point description:

CDAI-70 response was defined as a decrease in CDAI score of 70 or greater from baseline. The proportions of subjects with CDAI-70 response at Week 12 were compared between placebo and and PF-04236921 10 mg/50 mg. CDAI is used to quantify the symptoms of patients with Crohn's Disease. CDAI evaluates 8 Crohn's disease-related variables during a 1-week assessment period, yielding a composite score >=0 and without an upper limit. Many clinical trials use the endpoint for response as a 70 or greater point decrease in CDAI and clinical remission is often defined as a CDAI score below 150. Primary analysis: FAS excluding 200 mg arm (halted prematurely before reaching the planned sample size and thus no longer powered at the planned level to test against placebo).

End point type	Primary

End point timeframe:

Baseline and Week 12

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	Placebo	PF-04236921 10 milligram (mg)	PF-04236921 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	65	71	
Units: percentage of subjects				
least squares mean (confidence interval 90%)	28.6 (17.1 to 43.7)	35.2 (21.8 to 51.5)	47.4 (32.1 to 63.1)	

Statistical analyses

Statistical analysis title	Comparison between 10 mg and placebo at Week 12

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 10 milligram (mg)

Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[10]
P-value	= 0.2627 [11]
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	6.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-10.6
upper limit	23.9
Variability estimate	Standard error of the mean
Dispersion value	10.5

Notes:

[10] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.
[11] - Type I rate was controlled for the 2 time points (Week 8 and Week 12) at 0.05 (one sided).

Statistical analysis title	Comparison between 50 mg and placebo at Week 12

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[12]
P-value	= 0.0425 [13]
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	18.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.8
upper limit	36.7
Variability estimate	Standard error of the mean
Dispersion value	10.9

Notes:

[12] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.
[13] - Type I rate was controlled for the 2 time points (Week 8 and Week 12) at 0.05 (one sided).

Primary: The CDAI-70 response rate at Week 12 in subjects who received placebo and PF-04236921 200 mg

End point title	The CDAI-70 response rate at Week 12 in subjects who received placebo and PF-04236921 200 mg[14]

End point description:

CDAI-70 response was defined as a decrease in CDAI score of 70 or greater from baseline. The proportions of subjects with CDAI-70 response at Week 12 were compared between placebo and PF-04236921 200 mg. CDAI is used to quantify the symptoms of patients with Crohn's Disease. CDAI evaluates 8 Crohn's disease-related variables during a 1-week assessment period, yielding a composite score >=0 and without an upper limit. Many clinical trials use the endpoint for response as a 70 or greater point decrease in CDAI and clinical remission is often defined as a CDAI score below 150. The

analysis was performed on FAS 200 mg vs placebo. The 200 mg arm was halted before reaching the planned sample size of approximately 60 and was no longer powered at the planned level to test against placebo. Thus, the 200 mg vs placebo comparison is a sensitivity analysis.

End point type	Primary

End point timeframe:

Baseline and Week 12

Notes:

[14] - 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: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	Placebo	PF-04236921 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	40		
Units: percentage of subjects				
least squares mean (confidence interval 90%)	26.7 (14 to 44.9)	41.7 (21.2 to 65.6)		

Statistical analyses

Statistical analysis title	Comparison between 200 mg and placebo at Week 12

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference). Since the inputs in the model included different Analysis Population than in End Point 3, that will yield different estimates for placebo for the two different models.

Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[15]
P-value	= 0.1362 [16]
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	15.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.5
upper limit	37.6
Variability estimate	Standard error of the mean
Dispersion value	13.7

Notes:

[15] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.
[16] - Type I rate was controlled for the 2 time points (Week 8 and Week 12) at 0.05 (one sided).

Secondary: The CDAI-70 response rate over time in subjects who received placebo, PF-04236921 10 mg and PF-04236921 50 mg

End point title	The CDAI-70 response rate over time in subjects who received placebo, PF-04236921 10 mg and PF-04236921 50 mg[17]

End point description:

CDAI-70 response was defined as a decrease in CDAI score of 70 or greater from baseline. The proportions of subjects with CDAI-70 response were compared between placebo and PF-04236921 10 mg/50 mg. CDAI is used to quantify the symptoms of patients with Crohn's Disease. CDAI evaluates 8 Crohn's disease-related variables during a 1-week assessment period, yielding a composite score >=0 and without an upper limit. Many clinical trials use the endpoint for response as a 70 or greater point decrease in CDAI and clinical remission is often defined as a CDAI score below 150. The analysis was performed on the FAS excluding 200 mg arm (which was halted prematurely). "n" signifies the number of subjects with observed data of each arm at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 4, 6, and 10

Notes:

[17] - 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: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	Placebo	PF-04236921 10 milligram (mg)	PF-04236921 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	65	71	
Units: percentage of subjects				
least squares mean (confidence interval 90%)				
Week 2 (n=64, 63, 65)	12.3 (6.3 to 22.6)	19.4 (10.9 to 32.2)	18.1 (10.1 to 30.3)	
Week 4 (n=66, 58, 59)	16.5 (9 to 28.2)	34.6 (21.7 to 50.3)	37 (23.8 to 52.5)	
Week 6 (n=58, 53, 60)	21.1 (11.9 to 34.6)	35 (21.7 to 51.2)	46.2 (31.6 to 61.5)	
Week 10 (n=54, 50, 51)	29.3 (17.5 to 44.7)	38.9 (24.4 to 55.5)	54 (37.8 to 69.3)	

Statistical analyses

Statistical analysis title	Comparison between 10 mg and placebo at Week 2

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[18]
P-value	= 0.1527
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	7.1

Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.3
upper limit	18.6
Variability estimate	Standard error of the mean
Dispersion value	7

Notes:

[18] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 10 mg and placebo at Week 4

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[19]
P-value	= 0.0235
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	18.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	3.1
upper limit	33.2
Variability estimate	Standard error of the mean
Dispersion value	9.1

Notes:

[19] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 10 mg and placeboat Week 6

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[20]
P-value	= 0.0792
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	13.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.3
upper limit	30.2

Variability estimate	Standard error of the mean
Dispersion value	9.9

Notes:

[20] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 10 mg and placebo at Week 10

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[21]
P-value	= 0.1909
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	9.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.4
upper limit	27.6
Variability estimate	Standard error of the mean
Dispersion value	11

Notes:

[21] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 2

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[22]
P-value	= 0.1981
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	5.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.4
upper limit	17
Variability estimate	Standard error of the mean
Dispersion value	6.8

Notes:

[22] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 4

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[23]
P-value	= 0.0132
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	20.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	5.3
upper limit	35.8
Variability estimate	Standard error of the mean
Dispersion value	9.3

Notes:

[23] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 6

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[24]
P-value	= 0.0063
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	25.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	8.6
upper limit	41.7
Variability estimate	Standard error of the mean
Dispersion value	10.1

Notes:

[24] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 10

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 50 mg

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[25]
P-value	= 0.0138
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	24.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	6.2
upper limit	43.1
Variability estimate	Standard error of the mean
Dispersion value	11.2

Notes:

[25] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Secondary: The CDAI-70 response rate over time in subjects who received placebo and PF-04236921 200 mg

End point title	The CDAI-70 response rate over time in subjects who received placebo and PF-04236921 200 mg[26]

End point description:

CDAI-70 response was defined as a decrease in CDAI score of 70 or greater from baseline. The proportions of subjects with CDAI-70 response were compared between placebo and PF-04236921 200 mg. CDAI is used to quantify the symptoms of patients with Crohn's Disease. CDAI evaluates 8 Crohn's disease-related variables during a 1-week assessment period, yielding a composite score >=0 and without an upper limit. Many clinical trials use the endpoint for response as a 70 or greater point decrease in CDAI and clinical remission is often defined as a CDAI score below 150. The analysis was performed on the FAS 200 mg vs placebo. The 200 mg arm was halted before reaching the planned sample size of approximately 60 subjects. "n" signifies the number of subjects with observed data of each arm at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 4, 6, and 10

Notes:

[26] - 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: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	Placebo	PF-04236921 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	40		
Units: percentage of subjects				
least squares mean (confidence interval 90%)				
Week 2 (n=64, 36)	11.2 (5 to 23.1)	26.5 (12.3 to 48.2)		
Week 4 (n=66, 35)	15.2 (7.2 to 29.1)	24.6 (11.2 to 45.9)		
Week 6 (n=58, 32)	19.5 (9.6 to 35.6)	27.2 (12.4 to 49.8)		
Week 10 (n=54, 29)	27.2 (14.2 to 45.8)	46.3 (24.5 to 69.7)		

Statistical analyses

Statistical analysis title	Comparison between 200 mg and placebo at Week 2

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference). Since the inputs in the model included different Analysis Population than in End Point 5, that will yield different estimates for placebo for the two different models.

Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[27]
P-value	= 0.0662
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	15.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.4
upper limit	32.1
Variability estimate	Standard error of the mean
Dispersion value	10.2

Notes:

[27] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 200 mg and placebo at Week 4

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference). Since the inputs in the model included different Analysis Population than in End Point 5, that will yield different estimates for placebo for the two different models.

Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[28]
P-value	= 0.1708
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	9.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.9
upper limit	25.8

Variability estimate	Standard error of the mean
Dispersion value	10

Notes:

[28] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 200 mg and placebo at Week 6

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference). Since the inputs in the model included different Analysis Population than in End Point 5, that will yield different estimates for placebo for the two different models.

Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[29]
P-value	= 0.2416
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	7.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-10.5
upper limit	26
Variability estimate	Standard error of the mean
Dispersion value	11.1

Notes:

[29] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 200 mg and placebo at Week 10

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference). Since the inputs in the model included different Analysis Population than in End Point 5, that will yield different estimates for placebo for the two different models.

Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[30]
P-value	= 0.088
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	19.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.1
upper limit	42.3
Variability estimate	Standard error of the mean
Dispersion value	14.1

Notes:

[30] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Secondary: The CDAI remission rate over time in subjects who received placebo, PF-04236921 10 mg and PF-04236921 50 mg

End point title	The CDAI remission rate over time in subjects who received placebo, PF-04236921 10 mg and PF-04236921 50 mg[31]

End point description:

CDAI remission rate was defined as an absolute CDAI score less than (<) 150. The proportions of subjects with CDAI remission were compared between placebo and PF-04236921 10 mg/50 mg. CDAI is used to quantify the symptoms of patients with Crohn's Disease. CDAI evaluates 8 Crohn's disease-related variables during a 1-week assessment period, yielding a composite score >=0 and without an upper limit. Many clinical trials use the endpoint for response as a 70 or greater point decrease in CDAI and clinical remission is often defined as a CDAI score below 150. The analysis was performed on the FAS excluding 200 mg arm (which was halted prematurely). "n" signifies the number of subjects with observed data of each arm at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 4, 6, 8, 10, and 12

Notes:

[31] - 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: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	Placebo	PF-04236921 10 milligram (mg)	PF-04236921 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	65	71	
Units: percentage of subjects				
least squares mean (confidence interval 90%)				
Week 2 (n=64, 63, 68)	1.6 (0.3 to 9.1)	3.6 (1 to 12.3)	9.6 (4.1 to 20.7)	
Week 4 (n=66, 58, 62)	3.4 (0.9 to 11.6)	4.1 (1.1 to 13.6)	19.7 (10 to 35.1)	
Week 6 (n=58, 53, 63)	8.5 (3.3 to 20.3)	7.3 (2.6 to 19.2)	23.4 (12.5 to 39.6)	
Week 8 (n=58, 53, 58)	16.3 (7.6 to 31.7)	10.8 (4.4 to 24.4)	24.9 (13.3 to 41.7)	
Week 10 (n=54, 50, 54)	13.1 (5.6 to 27.7)	19.9 (9.4 to 37.2)	30.9 (17.2 to 49.2)	
Week 12 (n=57, 52, 57)	10.9 (4.5 to 24.1)	10.8 (4.4 to 24.5)	27.4 (14.9 to 44.9)	

Statistical analyses

Statistical analysis title	Comparison between 10 mg and placebo at Week 2

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 10 milligram (mg)

Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[32]
P-value	= 0.261
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.2
upper limit	7.2
Variability estimate	Standard error of the mean
Dispersion value	3.2

Notes:

[32] - Status of anti-TNF experience and concomitant immunosuppressant therapy were included as covariates.

Statistical analysis title	Comparison between 10 mg and placebo at Week 4

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[33]
P-value	= 0.4291
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	0.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.6
upper limit	7
Variability estimate	Standard error of the mean
Dispersion value	3.8

Notes:

[33] - Status of anti-TNF experience and concomitant immunosuppressant therapy were included as covariates.

Statistical analysis title	Comparison between 10 mg and placeboat Week 6

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 10 milligram (mg)

Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[34]
P-value	= 0.5791
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	-1.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-11
upper limit	8.6
Variability estimate	Standard error of the mean
Dispersion value	6

Notes:

[34] - Status of anti-TNF experience and concomitant immunosuppressant therapy were included as covariates.

Statistical analysis title	Comparison between 10 mg and placebo at Week 8

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[35]
P-value	= 0.7544
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	-5.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-18.8
upper limit	7.7
Variability estimate	Standard error of the mean
Dispersion value	8

Notes:

[35] - Status of anti-TNF experience and concomitant immunosuppressant therapy were included as covariates.

Statistical analysis title	Comparison between 10 mg and placebo at Week 10

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 10 milligram (mg)

Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[36]
P-value	= 0.2308
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	6.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.3
upper limit	21.9
Variability estimate	Standard error of the mean
Dispersion value	9.2

Notes:

[36] - Status of anti-TNF experience and concomitant immunosuppressant therapy were included as covariates.

Statistical analysis title	Comparison between 10 mg and placebo at Week 12

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[37]
P-value	= 0.5038
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	-0.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-11.8
upper limit	11.7
Variability estimate	Standard error of the mean
Dispersion value	7.1

Notes:

[37] - Status of anti-TNF experience and concomitant immunosuppressant therapy were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 2

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 50 mg

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[38]
P-value	= 0.0498
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	8
Confidence interval	
level	90 %
sides	2-sided
lower limit	0
upper limit	16
Variability estimate	Standard error of the mean
Dispersion value	4.9

Notes:

[38] - Status of anti-TNF experience and concomitant immunosuppressant therapy were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 4

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[39]
P-value	= 0.0155
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	16.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	3.9
upper limit	28.7
Variability estimate	Standard error of the mean
Dispersion value	7.6

Notes:

[39] - Status of anti-TNF experience and concomitant immunosuppressant therapy were included as covariates.

Statistical analysis title	Comparison between 50 mg and placeboat Week 6

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 50 mg

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[40]
P-value	= 0.0399
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	14.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.9
upper limit	28.9
Variability estimate	Standard error of the mean
Dispersion value	8.5

Notes:

[40] - Status of anti-TNF experience and concomitant immunosuppressant therapy were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 8

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[41]
P-value	= 0.1866
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	8.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.2
upper limit	24.3
Variability estimate	Standard error of the mean
Dispersion value	9.6

Notes:

[41] - Status of anti-TNF experience and concomitant immunosuppressant therapy were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 10

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 50 mg

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[42]
P-value	= 0.0415
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	17.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.9
upper limit	34.7
Variability estimate	Standard error of the mean
Dispersion value	10.3

Notes:

[42] - Status of anti-TNF experience and concomitant immunosuppressant therapy were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 12

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[43]
P-value	= 0.0408
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	16.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.9
upper limit	32.1
Variability estimate	Standard error of the mean
Dispersion value	9.5

Notes:

[43] - Status of anti-TNF experience and concomitant immunosuppressant therapy were included as covariates.

Secondary: The CDAI remission rate over time in subjects who received placebo and PF-04236921 200 mg

End point title	The CDAI remission rate over time in subjects who received placebo and PF-04236921 200 mg[44]

End point description:

CDAI remission rate was defined as an absolute CDAI score <150. The proportions of subjects with CDAI remission were compared between placebo and PF-04236921 200 mg. CDAI is used to quantify the symptoms of patients with Crohn's Disease. CDAI evaluates 8 Crohn's disease-related variables during a 1-week assessment period, yielding a composite score >=0 and without an upper limit. Many clinical trials use the endpoint for response as a 70 or greater point decrease in CDAI and clinical remission is often defined as a CDAI score below 150. The analysis was performed on the FAS 200 mg vs placebo. The 200 mg arm was halted before reaching the planned sample size of approximately 60 subjects. "n" signifies the number of subjects with observed data of each arm at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 4, 6, 8, 10, and 12

Notes:

[44] - 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: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	Placebo	PF-04236921 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	40		
Units: percentage of subjects				
least squares mean (confidence interval 90%)				
Week 2 (n=64, 36)	1.1 (0.2 to 7.2)	6.9 (1.8 to 23.1)		
Week 4 (n=66, 35)	2.4 (0.5 to 9.8)	5.1 (1.2 to 19.6)		
Week 6 (n=58, 32)	6.1 (1.9 to 18.1)	8.8 (2.4 to 27.6)		
Week 8 (n=58, 29)	11.9 (4.3 to 29.1)	8.8 (2.3 to 28.3)		
Week 10 (n=54, 29)	9.4 (3.2 to 24.9)	14.8 (4.6 to 38.5)		
Week 12 (n=57, 29)	7.8 (2.5 to 21.5)	11.8 (3.4 to 33.5)		

Statistical analyses

Statistical analysis title	Comparison between 200 mg and placebo at Week 2

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference). Since the inputs in the model included different Analysis Population than in End Point 7, that will yield different estimates for placebo for the two different models.

Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[45]
P-value	= 0.1342
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	5.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.8
upper limit	14.5
Variability estimate	Standard error of the mean
Dispersion value	5.3

Notes:

[45] - Status of anti-TNF experience and concomitant immunosuppressant therapy were included as covariates.

Statistical analysis title	Comparison between 200 mg and placebo at Week 4

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference). Since the inputs in the model included different Analysis Population than in End Point 7, that will yield different estimates for placebo for the two different models.

Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[46]
P-value	= 0.2623
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	2.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.3
upper limit	9.8
Variability estimate	Standard error of the mean
Dispersion value	4.3

Notes:

[46] - Status of anti-TNF experience and concomitant immunosuppressant therapy were included as covariates.

Statistical analysis title	Comparison between 200 mg and placeboat Week 6

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference). Since the inputs in the model included different Analysis Population than in End Point 7, that will yield different estimates for placebo for the two different models.

Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[47]
P-value	= 0.3324
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	2.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.7
upper limit	13.2
Variability estimate	Standard error of the mean
Dispersion value	6.3

Notes:

[47] - Status of anti-TNF experience and concomitant immunosuppressant therapy were included as covariates.

Statistical analysis title	Comparison between 200 mg and placebo at Week 8

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference). Since the inputs in the model included different Analysis Population than in End Point 7, that will yield different estimates for placebo for the two different models.

Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[48]
P-value	= 0.6637
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	-3.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-15.5
upper limit	9.1
Variability estimate	Standard error of the mean
Dispersion value	7.5

Notes:

[48] - Status of anti-TNF experience and concomitant immunosuppressant therapy were included as covariates.

Statistical analysis title	Comparison between 200 mg and placebo at Week 10

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference). Since the inputs in the model included different Analysis Population than in End Point 7, that will yield different estimates for placebo for the two different models.

Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[49]
P-value	= 0.2721
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	5.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.3
upper limit	20.2
Variability estimate	Standard error of the mean
Dispersion value	9

Notes:

[49] - Status of anti-TNF experience and concomitant immunosuppressant therapy were included as covariates.

Statistical analysis title	Comparison between 200 mg and placebo at Week 12

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis

(mean difference). Since the inputs in the model included different Analysis Population than in End Point 7, that will yield different estimates for placebo for the two different models.

Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[50]
P-value	= 0.3022
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.8
upper limit	16.9
Variability estimate	Standard error of the mean
Dispersion value	7.8

Notes:

[50] - Status of anti-TNF experience and concomitant immunosuppressant therapy were included as covariates.

Secondary: The CDAI-100 response rate over time in subjects who received placebo, PF-04236921 10 mg and PF-04236921 50 mg

End point title	The CDAI-100 response rate over time in subjects who received placebo, PF-04236921 10 mg and PF-04236921 50 mg[51]

End point description:

CDAI-100 response was defined as a decrease in CDAI score of 100 or greater from baseline. The proportions of subjects with CDAI-100 response at Week 12 were compared between placebo and PF-04236921 10 mg/50 mg. CDAI is used to quantify the symptoms of patients with Crohn's Disease. CDAI evaluates 8 Crohn's disease-related variables during a 1-week assessment period, yielding a composite score >=0 and without an upper limit. Many clinical trials use the endpoint for response as a 70 or greater point decrease in CDAI and clinical remission is often defined as a CDAI score below 150. The analysis was performed on the FAS excluding 200 mg arm (which was halted prematurely). "n" signifies the number of subjects with observed data of each arm at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 4, 6, 8, 10, and 12

Notes:

[51] - 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: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis

End point values	Placebo	PF-04236921 10 milligram (mg)	PF-04236921 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	65	71	
Units: percentage of subjects				
least squares mean (confidence interval 90%)				
Week 2 (n=64, 63, 65)	12.4 (6.1 to 23.7)	16.7 (8.8 to 29.7)	12.6 (6.2 to 24)	
Week 4 (n=66, 58, 59)	13 (6.5 to 24.4)	18.1 (9.5 to 31.9)	26.3 (15.1 to 41.8)	

Week 6 (n=58, 53, 60)	14.5 (7.2 to 26.9)	28.7 (16.4 to 45.1)	32.2 (19.5 to 48.2)	
Week 8 (n=58, 53, 56)	24.1 (13.4 to 39.3)	26.5 (14.9 to 42.6)	37.9 (23.7 to 54.5)	
Week 10 (n=54, 50, 51)	21 (11.2 to 35.8)	29.8 (17 to 46.8)	38.2 (23.6 to 55.3)	
Week 12 (n=57, 52, 54)	22.2 (12.1 to 37)	32.7 (19.2 to 49.7)	36.2 (22.2 to 52.9)	

Statistical analyses

Statistical analysis title	Comparison between 10 mg and placebo at Week 2

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[52]
P-value	= 0.2687
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	4.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.2
upper limit	15.8
Variability estimate	Standard error of the mean
Dispersion value	7

Notes:

[52] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 10 mg and placebo at Week 4

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[53]
P-value	= 0.246
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	5.1

Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.1
upper limit	17.3
Variability estimate	Standard error of the mean
Dispersion value	7.4

Notes:

[53] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 10 mg and placeboat Week 6

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[54]
P-value	= 0.0633
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	14.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.1
upper limit	29.5
Variability estimate	Standard error of the mean
Dispersion value	9.3

Notes:

[54] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 10 mg and placebo at Week 8

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[55]
P-value	= 0.4036
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	2.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-13.8
upper limit	18.6

Variability estimate	Standard error of the mean
Dispersion value	9.9

Notes:

[55] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 10 mg and placebo at Week 10

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[56]
P-value	= 0.1921
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	8.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.9
upper limit	25.6
Variability estimate	Standard error of the mean
Dispersion value	10.2

Notes:

[56] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 2

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[57]
P-value	= 0.4893
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	0.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-10.5
upper limit	10.9
Variability estimate	Standard error of the mean
Dispersion value	6.5

Notes:

[57] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 10 mg and placebo at Week 12

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[58]
P-value	= 0.1541
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	10.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.5
upper limit	27.5
Variability estimate	Standard error of the mean
Dispersion value	10.3

Notes:

[58] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 4

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[59]
P-value	= 0.0619
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	13.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.9
upper limit	27.7
Variability estimate	Standard error of the mean
Dispersion value	8.6

Notes:

[59] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 50 mg and placeboat Week 6

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 50 mg

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[60]
P-value	= 0.029
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	17.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	2.3
upper limit	33.1
Variability estimate	Standard error of the mean
Dispersion value	9.3

Notes:

[60] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 8

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[61]
P-value	= 0.0988
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	13.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.8
upper limit	31.4
Variability estimate	Standard error of the mean
Dispersion value	10.7

Notes:

[61] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 10

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 50 mg

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[62]
P-value	= 0.0549
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	17.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.5
upper limit	35
Variability estimate	Standard error of the mean
Dispersion value	10.8

Notes:

[62] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 12

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[63]
P-value	= 0.092
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	14
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.3
upper limit	31.3
Variability estimate	Standard error of the mean
Dispersion value	10.5

Notes:

[63] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Secondary: The CDAI-100 response rate over time in subjects who received placebo and PF-04236921 200 mg

End point title	The CDAI-100 response rate over time in subjects who received placebo and PF-04236921 200 mg[64]

End point description:

CDAI-100 response was defined as a decrease in CDAI score of 100 or greater from baseline. The proportions of subjects with CDAI-100 response at Week 12 were compared between placebo and PF-04236921 200 mg. CDAI is used to quantify the symptoms of patients with Crohn's Disease. CDAI evaluates 8 Crohn's disease-related variables during a 1-week assessment period, yielding a composite score >=0 and without an upper limit. Many clinical trials use the endpoint for response as a 70 or greater point decrease in CDAI and clinical remission is often defined as a CDAI score below 150. The analysis was performed on the FAS 200 mg vs placebo. The 200 mg arm was halted before reaching the planned sample size of approximately 60 subjects. "n" signifies the number of subjects with observed data of each arm at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 4, 6, 8, 10, and 12

Notes:

[64] - 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: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis

End point values	Placebo	PF-04236921 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	40		
Units: percentage of subjects				
least squares mean (confidence interval 90%)				
Week 2 (n=64, 36)	10.3 (4.4 to 22.6)	12 (4.5 to 28.6)		
Week 4 (n=66, 35)	11 (4.7 to 23.5)	22.1 (9.5 to 43.5)		
Week 6 (n=58, 32)	12.2 (5.3 to 25.8)	22.2 (9.3 to 44.2)		
Week 8 (n=58, 29)	21.3 (10.3 to 39.1)	18.7 (7.3 to 40.2)		
Week 10 (n=54, 29)	18.2 (8.4 to 34.9)	30.4 (13.6 to 54.8)		
Week 12 (n=57, 29)	19.4 (9.2 to 36.5)	26.9 (11.6 to 50.6)		

Statistical analyses

Statistical analysis title	Comparison between 200 mg and placebo at Week 2

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference). Since the inputs in the model included different Analysis Population than in End Point 9, that will yield different estimates for placebo for the two different models.

Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[65]
P-value	= 0.4031
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	1.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.5
upper limit	12.9
Variability estimate	Standard error of the mean
Dispersion value	6.8

Notes:

[65] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 200 mg and placebo at Week 4

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference). Since the inputs in the model included different Analysis Population than in End Point 9, that will yield different estimates for placebo for the two different models.

Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[66]
P-value	= 0.1219
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	11.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.6
upper limit	26.8
Variability estimate	Standard error of the mean
Dispersion value	9.6

Notes:

[66] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 200 mg and placeboat Week 6

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference). Since the inputs in the model included different Analysis Population than in End Point 9, that will yield different estimates for placebo for the two different models.

Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[67]
P-value	= 0.16
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	9.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.5
upper limit	26.4
Variability estimate	Standard error of the mean
Dispersion value	10

Notes:

[67] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 200 mg and placebo at Week 8

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference). Since the inputs in the model included different Analysis Population than in End Point 9, that will yield different estimates for placebo for the two different models.

Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[68]
P-value	= 0.6019
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	-2.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-19.5
upper limit	14.2
Variability estimate	Standard error of the mean
Dispersion value	10.3

Notes:

[68] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 200 mg and placebo at Week 10

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference). Since the inputs in the model included different Analysis Population than in End Point 9, that will yield different estimates for placebo for the two different models.

Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[69]
P-value	= 0.1601
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	12.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8
upper limit	32.5
Variability estimate	Standard error of the mean
Dispersion value	12.3

Notes:

[69] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 200 mg and placebo at Week 12

Statistical analysis description:

The Outcome included a Generalized linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis

(mean difference). Since the inputs in the model included different Analysis Population than in End Point 9, that will yield different estimates for placebo for the two different models.

Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[70]
P-value	= 0.2622
Method	GLMM
Parameter estimate	Mean difference (final values)
Point estimate	7.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-11.8
upper limit	26.6
Variability estimate	Standard error of the mean
Dispersion value	11.7

Notes:

[70] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Secondary: Change from baseline in CDAI score over time in subjects who received placebo, PF-04236921 10 mg and PF-04236921 50 mg

End point title	Change from baseline in CDAI score over time in subjects who received placebo, PF-04236921 10 mg and PF-04236921 50 mg[71]

End point description:

CDAI evaluates 8 Crohn's disease-related variables during a 1-week assessment period, yielding a composite score >=0 and without an upper limit, and higher score indicate more severe disease. The Outcome included a Linear mixed model analyses which incorporated longitudinal data for each subject, and the same model is used for estimate (least squares mean) and statistical analysis (mean difference).

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 4, 6, 8, 10, and 12

Notes:

[71] - 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: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis

End point values	Placebo	PF-04236921 10 milligram (mg)	PF-04236921 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	65	71	
Units: points on a scale				
least squares mean (confidence interval 90%)				
Week 2 (n=64, 63, 65)	-18.9 (-38.3 to 0.6)	-28.4 (-47.6 to -9.3)	-16.2 (-34.5 to 2.2)	
Week 4 (n=66, 58, 59)	-25.1 (-44.9 to -5.2)	-37.1 (-57 to -17.1)	-50.7 (-70 to -31.5)	
Week 6 (n=58, 53, 60)	-32.6 (-55.5 to -9.6)	-48.5 (-71.7 to -25.3)	-54.9 (-77 to -32.9)	
Week 8 (n=58, 53, 56)	-34.6 (-58.8 to -10.5)	-49.6 (-74.1 to -25)	-63.5 (-86.9 to -40)	

Week 10 (n=54, 50, 51)	-19.8 (-45.9 to 6.4)	-50 (-76.6 to -23.4)	-64.7 (-90.3 to -39.1)	
Week 12 (n=57, 52, 54)	-27.3 (-53.5 to -1.2)	-44.2 (-70.9 to -17.5)	-66.8 (-92.5 to -41.2)	

Statistical analyses

Statistical analysis title	Comparison between 10 mg and placebo at Week 2
Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[72]
P-value	= 0.2173
Method	Linear mixed model (LMM)
Parameter estimate	Mean difference (final values)
Point estimate	-9.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-29.8
upper limit	10.6
Variability estimate	Standard error of the mean
Dispersion value	12.22

Notes:

[72] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 10 mg and placebo at Week 4
Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[73]
P-value	= 0.1778
Method	LMM
Parameter estimate	Mean difference (final values)
Point estimate	-12
Confidence interval	
level	90 %
sides	2-sided
lower limit	-33.4
upper limit	9.4
Variability estimate	Standard error of the mean
Dispersion value	12.95

Notes:

[73] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 10 mg and placeboat Week 6
Comparison groups	Placebo v PF-04236921 10 milligram (mg)

Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[74]
P-value	= 0.1661
Method	LMM
Parameter estimate	Mean difference (final values)
Point estimate	-15.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-43
upper limit	11.2
Variability estimate	Standard error of the mean
Dispersion value	16.37

Notes:

[74] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 10 mg and placebo at Week 8
Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[75]
P-value	= 0.1993
Method	LMM
Parameter estimate	Mean difference (final values)
Point estimate	-14.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-44.1
upper limit	14.3
Variability estimate	Standard error of the mean
Dispersion value	17.66

Notes:

[75] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 10 mg and placebo at Week 10
Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[76]
P-value	= 0.0632
Method	LMM
Parameter estimate	Mean difference (final values)
Point estimate	-30.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-62.7
upper limit	2.3

Variability estimate	Standard error of the mean
Dispersion value	19.66

Notes:

[76] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 10 mg and placebo at Week 12
Comparison groups	Placebo v PF-04236921 10 milligram (mg)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other[77]
P-value	= 0.1975
Method	LMM
Parameter estimate	Mean difference (final values)
Point estimate	-16.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-49.4
upper limit	15.8
Variability estimate	Standard error of the mean
Dispersion value	19.71

Notes:

[77] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 2
Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[78]
P-value	= 0.5868
Method	LMM
Parameter estimate	Mean difference (final values)
Point estimate	2.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-17.6
upper limit	22.9
Variability estimate	Standard error of the mean
Dispersion value	12.25

Notes:

[78] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 4
Comparison groups	Placebo v PF-04236921 50 mg

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[79]
P-value	= 0.0243
Method	LMM
Parameter estimate	Mean difference (final values)
Point estimate	-25.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-47
upper limit	-4.3
Variability estimate	Standard error of the mean
Dispersion value	12.93

Notes:

[79] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 50 mg and placeboat Week 6
Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[80]
P-value	= 0.0834
Method	LMM
Parameter estimate	Mean difference (final values)
Point estimate	-22.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-49
upper limit	4.3
Variability estimate	Standard error of the mean
Dispersion value	16.12

Notes:

[80] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 8
Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[81]
P-value	= 0.0499
Method	LMM
Parameter estimate	Mean difference (final values)
Point estimate	-28.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-57.7
upper limit	0

Variability estimate	Standard error of the mean
Dispersion value	17.43

Notes:

[81] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 10
Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[82]
P-value	= 0.0111
Method	LMM
Parameter estimate	Mean difference (final values)
Point estimate	-44.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-77.1
upper limit	-12.7
Variability estimate	Standard error of the mean
Dispersion value	19.45

Notes:

[82] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 50 mg and placebo at Week 12
Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[83]
P-value	= 0.0221
Method	LMM
Parameter estimate	Mean difference (final values)
Point estimate	-39.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-71.7
upper limit	-7.3
Variability estimate	Standard error of the mean
Dispersion value	19.49

Notes:

[83] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Secondary: Change from baseline in CDAI score over time in subjects who received placebo and PF-04236921 200 mg

End point title	Change from baseline in CDAI score over time in subjects who received placebo and PF-04236921 200 mg[84]

End point description:

CDAI evaluates 8 Crohn's disease-related variables during a 1-week assessment period, yielding a composite score >=0 and without an upper limit, and higher score indicate more severe disease. The Outcome included a Linear mixed model analyses which incorporated longitudinal data for each subject,

and the same model is used for estimate (least squares mean) and statistical analysis (mean difference). Since the inputs in the model included different Analysis Population than in End Point 11, that will yield different estimates for placebo for the two different models.

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 4, 6, 8, 10, and 12

Notes:

[84] - 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: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis

End point values	Placebo	PF-04236921 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	40		
Units: points on a scale				
least squares mean (confidence interval 90%)				
Week 2 (n=64, 36)	-21.3 (-49.1 to 6.6)	-30.1 (-62.2 to 2.1)		
Week 4 (n=66, 35)	-26.6 (-54.3 to 1.1)	-30.5 (-62.5 to 1.6)		
Week 6 (n=58, 32)	-36.7 (-64.6 to -8.7)	-42.2 (-74.8 to -9.6)		
Week 8 (n=58, 29)	-39.1 (-67.2 to -11)	-48.1 (-81.3 to -14.9)		
Week 10 (n=54, 29)	-26.3 (-54.7 to 2.1)	-56.1 (-89.5 to -22.7)		
Week 12 (n=57, 29)	-35.2 (-63.6 to -6.8)	-66.2 (-99.9 to -32.6)		

Statistical analyses

Statistical analysis title	Comparison between 200 mg and placebo at Week 2
Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[85]
P-value	= 0.3157
Method	LMM
Parameter estimate	Mean difference (final values)
Point estimate	-8.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-39
upper limit	21.4
Variability estimate	Standard error of the mean
Dispersion value	18.27

Notes:

[85] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 200 mg and placebo at Week 4
Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[86]
P-value	= 0.4171
Method	LMM
Parameter estimate	Mean difference (final values)
Point estimate	-3.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-34
upper limit	26.4
Variability estimate	Standard error of the mean
Dispersion value	18.28

Notes:

[86] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 200 mg and placeboat Week 6
Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[87]
P-value	= 0.3837
Method	LMM
Parameter estimate	Mean difference (final values)
Point estimate	-5.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-36.6
upper limit	25.5
Variability estimate	Standard error of the mean
Dispersion value	18.79

Notes:

[87] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 200 mg and placebo at Week 8
Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[88]
P-value	= 0.3204
Method	LMM
Parameter estimate	Mean difference (final values)
Point estimate	-9

Confidence interval	
level	90 %
sides	2-sided
lower limit	-40.8
upper limit	22.8
Variability estimate	Standard error of the mean
Dispersion value	19.27

Notes:

[88] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 200 mg and placebo at Week 10
Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[89]
P-value	= 0.0649
Method	LMM
Parameter estimate	Mean difference (final values)
Point estimate	-29.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-62.3
upper limit	2.6
Variability estimate	Standard error of the mean
Dispersion value	19.64

Notes:

[89] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Statistical analysis title	Comparison between 200 mg and placebo at Week 12
Comparison groups	Placebo v PF-04236921 200 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[90]
P-value	= 0.0598
Method	LMM
Parameter estimate	Mean difference (final values)
Point estimate	-31
Confidence interval	
level	90 %
sides	2-sided
lower limit	-63.9
upper limit	1.8
Variability estimate	Standard error of the mean
Dispersion value	19.87

Notes:

[90] - Status of anti-TNF experience, concomitant immunosuppressant therapy, and baseline were included as covariates.

Secondary: Percentages of subjects with confirmed positive anti-drug antibodies (ADAs)

End point title	Percentages of subjects with confirmed positive anti-drug antibodies (ADAs)[91]

End point description:

The percentage of subjects with confirmed positive ADA was summarized for each treatment arm. ADA positive was defined as ADA titer (ie, the reciprocal of the highest dilution that gave a value equivalent to the cut point of the assay) >= 4.32. The SAS consisted of all subjects who received at least 1 dose of study drug. "n" signifies number of subjects with observed data at the time point of each arm. From Weeks 16 to 40, only subjects who remained in the follow-up period of this study and did not enter NCT01405196 were analyzed. "99999" signifies no subjects were analyzed at the time point in the treatment arm and therefore data was not available.

End point type	Secondary

End point timeframe:

At baseline (Day 1) and at Weeks 4, 8, 12, 16, 24, 32 and 40

Notes:

[91] - 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: Subjects in the placebo arm did not receive the study drug PF-04236921. Only subjects in the active treatment arms (PF-04236921) were analyzed for ADAs.

End point values	PF-04236921 10 milligram (mg)	PF-04236921 50 mg	PF-04236921 200 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	71	40	
Units: percentage of subjects				
number (not applicable)				
Day 1 (n=56, 66, 36)	0	0	0	
Week 4 (n=58, 62, 29)	0	1.6	0	
Week 8 (n=53, 53, 27)	0	0	0	
Week 12 (n=46, 49, 24)	0	0	0	
Week 16 (n=2, 1, 0)	0	0	99999	
Week 24 (n=2, 1, 0)	0	0	99999	
Week 32 (n=1, 0, 0)	0	99999	99999	
Week 40 (n=2, 1, 0)	0	0	99999	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with confirmed positive neutralizing antibodies (NAbs)

End point title	Percentages of subjects with confirmed positive neutralizing antibodies (NAbs)[92]

End point description:

The percentage of subjects with confirmed positive NAbs was summarized for each treatment arm. Only ADA positive samples were analyzed for NAb. A multi-tiered approach was utilized to detect NAbs. NAb serum samples were screened at tier one, and those found presumptively NAb positive was further tested with the confirmatory assay (tier two). The percentage of subjects with confirmed positive NAbs was summarized for each treatment.

End point type	Secondary

End point timeframe:

At baseline (Day 1) and at Weeks 4, 8, 12, 16, 24, 32 and 40

Notes:

[92] - 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: Subjects in the placebo arm did not receive the study drug PF-04236921. Only subjects in the active treatment arms (PF-04236921) were analyzed for ADAs and only ADA positive samples were analyzed for NAbs.

End point values	PF-04236921 10 milligram (mg)	PF-04236921 50 mg	PF-04236921 200 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	71	40	
Units: percentage of subjects				
number (not applicable)				
Day 1 (n=56, 66, 36)	0	0	0	
Week 4 (n=58, 62, 29)	0	1.6	0	
Week 8 (n=53, 53, 27)	0	0	0	
Week 12 (n=46, 49, 24)	0	0	0	
Week 16 (n=2, 1, 0)	0	0	99999	
Week 24 (n=2, 1, 0)	0	0	99999	
Week 32 (n=1, 0, 0)	0	99999	99999	
Week 40 (n=2, 1, 0)	0	0	99999	

Statistical analyses

No statistical analyses for this end point

Secondary: Serum PF-04236921 concentration over time

End point title	Serum PF-04236921 concentration over time[93]

End point description:

The pharmacokinetic (PK) analysis set was the subset of subjects from the SAS who provided at least 1 PK concentration (2 subjects [10 mg arm] excluded due to a quality issue). "n" is the number of subjects with PK data at the visit. From Weeks 16 to 40, only subjects who remained in the follow-up period of this study were analyzed. "99999"=value not available, due to reasons including 1) arithmetic mean not available due to all samples were below the lower limit of quantification (<LLOQ) and thus no concentrations could be determined at the visit; 2) arithmetic mean was not available due to the number of subject analzyed was 0 at the visit; 3) Standard deviation was not calculable as there was only 1 subject.

End point type	Secondary

End point timeframe:

Day 1 (predose), and at Weeks 2, 4 (Day 28, predose), 8, 10, 12, 16, 20, 24, 28, 32, 36, and 40

Notes:

[93] - 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: Subjects in the placebo arm did not receive the study drug PF-04236921. Only subjects in the active treatment arms (PF-04236921) were analyzed for serum PF 04236921 concentration.

End point values	PF-04236921 10 milligram (mg)	PF-04236921 50 mg	PF-04236921 200 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	71	40	
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Day 1 (n=54, 64, 37)	4.52 (± 33.2)	2.05 (± 16.38)	99999 (± 99999)	
Week 2 (n=46, 56, 30)	1060 (± 531.3)	4580 (± 1938)	21300 (± 9547)	
Week 4 (n=56, 63, 29)	674 (± 339.3)	3180 (± 1555)	14800 (± 6641)	
Week 6 (n=48, 57, 28)	1470 (± 863)	6610 (± 2668)	32200 (± 13240)	
Week 8 (n=51, 52, 28)	992 (± 501.7)	4500 (± 1993)	20200 (± 8683)	
Week 10 (n=47, 54, 29)	695 (± 428.5)	3280 (± 1961)	13600 (± 7350)	
Week 12 (n=43, 51, 26)	504 (± 435.5)	2110 (± 1333)	10900 (± 7802)	
Week 16 (n=2, 1, 0)	177 (± 250.3)	1290 (± 99999)	99999 (± 99999)	
Week 20 (n=2, 1, 0)	102 (± 143.5)	425 (± 99999)	99999 (± 99999)	
Week 24 (n=2, 1, 0)	63.5 (± 89.8)	99999 (± 99999)	99999 (± 99999)	
Week 28 (n=2, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Week 32 (n=2, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Week 36 (n=2, 1, 0)	99999 (± 99999)	109 (± 99999)	99999 (± 99999)	
Week 40 (n=2, 1, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects who withdrew from the study due to treatment-emergent adverse events (AEs)

End point title	Number of subjects who withdrew from the study due to treatment-emergent adverse events (AEs)

End point description:

An AE was any untoward medical occurrence without regard to causality in a subject who received study drug. Treatment-emergent were events between first dose of treatment and up to 28 days after last dose that were absent before treatment or that worsened relative to pretreatment state. The SAS consisted of all subjects who received at least 1 dose of study drug. "n" signifies number of subjects with observed data at the time point of each arm. From Weeks 16 to 40, only subjects who remained in the follow-up period of this study and did not enter NCT01405196 were analyzed.

End point type	Secondary

End point timeframe:

Induction period: from Week 0 (Day 1) through Week 12; follow-up period: from Week 12 (or discontinuation from the induction period) through last subject visit (up to 28 weeks after completion of or discontinuation from the 12-week induction period)

End point values	Placebo	PF-04236921 10 milligram (mg)	PF-04236921 50 mg	PF-04236921 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	67	71	40
Units: subjects				
number (not applicable)				
Induction period (Weeks 0 to 12)	7	6	6	8
Follow-up period (after Week 12)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The reporting period was from the time of the first dose of study treatment through last subject visit up to 40 weeks post the first dose of study treatment for serious adverse events (SAEs) and non serious adverse events (AEs).

Adverse event reporting additional description:

The same event may appear as both a non serious AE and an SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as non-serious in another subject, or one subject may have experienced both a serious and non-serious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Placebo administered SC in the anterolateral right and left thighs on Day 1 and Day 28. Each subject received 2 injections due to the double-dummy design of the study.

Reporting group title	PF-04236921 200 mg

Reporting group description:

PF-04236921 200 mg administered SC in the anterolateral right and left thighs on Day 1 and Day 28. Each subject received 2 injections due to the double-dummy design of the study.

Reporting group title	PF-04236921 50 mg

Reporting group description:

PF-04236921 50 mg administered SC in the anterolateral right and left thighs on Day 1 and Day 28. Each subject received 2 injections due to the double-dummy design of the study.

Reporting group title	PF-04236921 10 mg

Reporting group description:

PF-04236921 10 mg administered SC in the anterolateral right and left thighs on Day 1 and Day 28. Each subject received 2 injections due to the double-dummy design of the study.

Serious adverse events	Placebo	PF-04236921 200 mg	PF-04236921 50 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 69 (15.94%)	11 / 40 (27.50%)	12 / 71 (16.90%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test abnormal			

subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	1 / 69 (1.45%)	0 / 40 (0.00%)	0 / 71 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 40 (2.50%)	0 / 71 (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
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIIth nerve paralysis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 40 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device occlusion			

subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	1 / 69 (1.45%)	0 / 40 (0.00%)	0 / 71 (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
Pyrexia			
subjects affected / exposed	1 / 69 (1.45%)	0 / 40 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 69 (0.00%)	1 / 40 (2.50%)	2 / 71 (2.82%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 40 (0.00%)	0 / 71 (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
Crohn’s disease			
subjects affected / exposed	6 / 69 (8.70%)	4 / 40 (10.00%)	5 / 71 (7.04%)
occurrences causally related to treatment / all	1 / 7	0 / 4	2 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			

subjects affected / exposed	0 / 69 (0.00%)	1 / 40 (2.50%)	0 / 71 (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
Ileal fistula			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 69 (0.00%)	1 / 40 (2.50%)	0 / 71 (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
Large intestinal stenosis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 69 (0.00%)	1 / 40 (2.50%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 69 (0.00%)	1 / 40 (2.50%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			

subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 40 (2.50%)	0 / 71 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	1 / 69 (1.45%)	0 / 40 (0.00%)	0 / 71 (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			
Abscess			
subjects affected / exposed	1 / 69 (1.45%)	0 / 40 (0.00%)	0 / 71 (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
Abscess intestinal			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	2 / 71 (2.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Groin abscess			
subjects affected / exposed	0 / 69 (0.00%)	1 / 40 (2.50%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal abscess			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 69 (0.00%)	1 / 40 (2.50%)	0 / 71 (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
Retroperitoneal abscess			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 40 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Malnutrition			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	PF-04236921 10 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 67 (16.42%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Liver function test abnormal			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
VIIth nerve paralysis			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chills			

subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device occlusion				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Vertigo positional				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	2 / 67 (2.99%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Anal fistula				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Crohn’s disease				

subjects affected / exposed	6 / 67 (8.96%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 0			
Haematochezia				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileal fistula				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal perforation				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestinal stenosis				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestine perforation				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Atelectasis				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				

subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fistula				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abscess				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abscess intestinal				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Anal abscess				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Groin abscess				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Perirectal abscess				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retroperitoneal abscess				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Malnutrition				
subjects affected / exposed	0 / 67 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	Placebo	PF-04236921 200 mg	PF-04236921 50 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 69 (52.17%)	20 / 40 (50.00%)	48 / 71 (67.61%)
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 69 (8.70%)	2 / 40 (5.00%)	9 / 71 (12.68%)
occurrences (all)	9	3	13
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 69 (5.80%)	2 / 40 (5.00%)	2 / 71 (2.82%)
occurrences (all)	4	2	2
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	4 / 71 (5.63%)
occurrences (all)	0	0	4
Pyrexia			
subjects affected / exposed	7 / 69 (10.14%)	1 / 40 (2.50%)	5 / 71 (7.04%)
occurrences (all)	7	1	7
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	8 / 69 (11.59%)	6 / 40 (15.00%)	8 / 71 (11.27%)
occurrences (all)	8	7	8
Abdominal pain upper			
subjects affected / exposed	0 / 69 (0.00%)	3 / 40 (7.50%)	1 / 71 (1.41%)
occurrences (all)	0	3	1
Crohn’s disease			
subjects affected / exposed	4 / 69 (5.80%)	4 / 40 (10.00%)	7 / 71 (9.86%)
occurrences (all)	5	4	7
Nausea			
subjects affected / exposed	1 / 69 (1.45%)	1 / 40 (2.50%)	7 / 71 (9.86%)
occurrences (all)	1	1	9
Proctalgia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 40 (0.00%)	5 / 71 (7.04%)
occurrences (all)	0	0	5
Vomiting			

subjects affected / exposed	2 / 69 (2.90%)	2 / 40 (5.00%)	5 / 71 (7.04%)
occurrences (all)	2	2	6
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 69 (0.00%)	1 / 40 (2.50%)	5 / 71 (7.04%)
occurrences (all)	0	2	6
Rash			
subjects affected / exposed	1 / 69 (1.45%)	1 / 40 (2.50%)	7 / 71 (9.86%)
occurrences (all)	1	1	9
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 69 (11.59%)	0 / 40 (0.00%)	5 / 71 (7.04%)
occurrences (all)	8	0	5
Back pain			
subjects affected / exposed	4 / 69 (5.80%)	1 / 40 (2.50%)	3 / 71 (4.23%)
occurrences (all)	4	1	3
Pain in extremity			
subjects affected / exposed	4 / 69 (5.80%)	1 / 40 (2.50%)	1 / 71 (1.41%)
occurrences (all)	4	1	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 69 (4.35%)	3 / 40 (7.50%)	8 / 71 (11.27%)
occurrences (all)	3	4	8
Upper respiratory tract infection			
subjects affected / exposed	2 / 69 (2.90%)	0 / 40 (0.00%)	4 / 71 (5.63%)
occurrences (all)	2	0	4
Urinary tract infection			
subjects affected / exposed	3 / 69 (4.35%)	5 / 40 (12.50%)	3 / 71 (4.23%)
occurrences (all)	3	8	3

Non-serious adverse events	PF-04236921 10 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 67 (56.72%)		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 67 (5.97%)		
occurrences (all)	7		

Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	 1 / 67 (1.49%) 1		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 2 / 67 (2.99%) 2 5 / 67 (7.46%) 6		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Crohn’s disease subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Proctalgia subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 6 / 67 (8.96%) 6 1 / 67 (1.49%) 1 2 / 67 (2.99%) 4 8 / 67 (11.94%) 9 2 / 67 (2.99%) 3 4 / 67 (5.97%) 4		
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all) Rash	 1 / 67 (1.49%) 1 		

subjects affected / exposed	3 / 67 (4.48%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 67 (7.46%)		
occurrences (all)	9		
Back pain			
subjects affected / exposed	4 / 67 (5.97%)		
occurrences (all)	4		
Pain in extremity			
subjects affected / exposed	2 / 67 (2.99%)		
occurrences (all)	2		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	11 / 67 (16.42%)		
occurrences (all)	11		
Upper respiratory tract infection			
subjects affected / exposed	0 / 67 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	4 / 67 (5.97%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 March 2011	Amendment 1 occurred on 03 March 2011. Changes were made to Exclusion Criteria 3, 17, 21 and 22. Exclusion Criterion 3 was modified adding subjects with total colectomy with ileorectal anastomosis, multiple small bowel re-section resulting in malabsorption or the need for total parenteral nutrition. Exclusion Criterion 17 was modified to allow oral ibuprofen use to less than or equal to 800 mg/day as needed. Exclusion Criterion 21 was updated to include "experimental biologics", that had or had not been indicated for Crohn's disease (eg, vedolizumab, abatacept, etc), or received marketing approval during this study, unless the subject's last dose was greater than or equal to 12 months at screening. Exclusion Criterion 22, modified to indicate that the prohibition of use of bismuth subsalicylate products was after signing the informed consent. In Section 9.4, language was added to allow for an early pharmacokinetics (PK) readout after 24 to 32 subjects (6 to 8 per treatment) had their Week 4 PK sample analyzed.
02 February 2012	Amendment 2 occurred on 02 February 2012. The duration of the study enrollment was changed from 12 to 21 months, the number of sites increased from 100 to approximately 160 and completion time for the study was changed to approximately 32 months versus 24 months. Inclusion Criterion 5 was revised requiring a 2-week stable dose prior to randomization for subjects on mesalamine, oral steroids and/or immunosuppressants. Exclusion Criterion 14, Clostridium difficile testing was updated to ensure sensitivity testing is completed per recent practice guidelines. Exclusion Criterion 21, added information that biologics do not include anti-tumor necrosis factors (anti-TNFs). The washout period for anti-TNFs was changed to 6 weeks from 30 days/5 half-lives (whichever was longer).
20 September 2012	Amendment 3 occurred on 20 September 2012, and incorporated the removal of the Prometheus inflammatory bowel disease (IBD) biomarker as an exploratory endpoint. Sample size determination was revised to accommodate the interim futility analysis. Clarification was provided on missing data imputation, and the description of the interim analysis plan was added as well as noting the external Data Monitoring Committee would review the results of the analysis. For the secondary pharmacodynamic (PD) objective, removed "mean" from change of baseline for PD markers to allow for flexibility (ie, median or mean percentage change). Added "genotype" to specify the type of thiopurine S-methyltransferase (TPMT) test. For approximate duration of study, enrollment was changed from 21 months to 30 months; and study completion was changed from approximately 32 months to 41 months due to enrollment extension. For Inclusion Criterion 7, added historical colonoscopy within 8 weeks prior to screening documenting ulceration and retrospectively completing the Simple Endoscopic Score for Crohn's Disease (SES-CD) as acceptable. For Exclusion Criterion 2, clarified requirement for computed tomography (CT) or magnetic resonance (MR) enterography and added definition of active fistulae. Exclusion Criterion 27, newly added that "Subjects with known allergy or hypersensitivity to the investigational product or its components" were to be excluded.
27 February 2013	Amendment 4 occurred on 27 February 2013 to address the changes in tuberculosis (TB) testing as a result of a special safety concern that occurred in the B0151006 study investigating PF-04236921 for the indication of systemic lupus erythematosus (SLE). TB testing was also recommended for subjects undergoing certain steroid regimens. Baseline window was extended from 7 days to 10 days.

22 August 2013	Amendment 5 occurred on 22 August 2013 to stop further enrollment in the 200 mg dosing arm, as well as any further dosing in the 200 mg arm. The External Data Monitoring Committee (E-DMC) recommended that the 200 mg dose be halted in the B0151003 study as a precaution since there were safety concerns in the Lupus population utilizing the same compound at 200 mg. Statistical sections modified to reflect change in study design. Language was added throughout the protocol along with recommendations and instructions for how these subjects would be followed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Enrollment into the 200 mg arm was halted on 14 August 2013 before reaching the planned sample size due to safety findings in NCT01405196. Hence the 200 mg vs placebo comparisons were excluded from the primary analyses and reported separately.

Notes: