Clinical trial results:
A Multicenter Open-Label Extension Study to Assess Long-Term Safety of PF-00547659 in Subjects With Crohn's Disease (OPERA II)

Summary

EudraCT number	2010-024638-48
Trial protocol	SK BE SE AT PT DE NO NL ES PL BG Outside EU/EEA
Global end of trial date	27 July 2016

Results information

Result version number	v1 (current)
This version publication date	11 August 2017
First version publication date	11 August 2017

Trial information

Trial identification

Sponsor protocol code	A7281007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01298492
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Shire
Sponsor organisation address	300 Shire Way, Lexington, MA, United States, 02421
Public contact	Study Physician, Shire, 1 866-842-5335,
Scientific contact	Study Physician, Shire, 1 866-842-5335,

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	27 July 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to monitor the safety and tolerability of PF-00547659 during long-term treatment.

Protection of trial subjects:

This study was conducted in accordance with current applicable regulations, International Council for Harmonisation (ICH) of Good Clinical Practice, the principles of the Declaration of Helsinki, as well as other applicable local ethical and legal requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 July 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 17
Country: Number of subjects enrolled	Belgium: 25
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	France: 18
Country: Number of subjects enrolled	Germany: 24
Country: Number of subjects enrolled	Japan: 8
Country: Number of subjects enrolled	Korea, Republic of: 9
Country: Number of subjects enrolled	Netherlands: 36
Country: Number of subjects enrolled	Norway: 5
Country: Number of subjects enrolled	Poland: 13
Country: Number of subjects enrolled	Serbia: 14
Country: Number of subjects enrolled	Slovakia: 8
Country: Number of subjects enrolled	South Africa: 4
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	United States: 72
Worldwide total number of subjects	268
EEA total number of subjects	154

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)	265
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 81 centers in Austria, Belgium, Canada, France, Germany, Japan, Netherlands, Norway, Poland, Republic of Korea, Serbia, Slovakia, South Africa, Spain and United States between 22 July 2011 (first subject first visit) and 27 July 2016 (last subject last visit).

Pre-assignment

Screening details:

A total of 268 subjects (225 subjects from Feeder Study A7281006 [NCT01276509] and 43 subjects from Feeder Study A7281008 [NCT01387594]) were enrolled and overall 149 subjects completed the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	PF-00547659 75 mg

Arm description:

Subjects received PF-00547659 75 mg subcutaneous injection once in every 4 weeks through Week 72. One time dose escalation to 225 mg subcutaneous injection was allowed after 8 weeks of the study for the subjects who experienced clinical deterioration or unacceptably low level of response to study drug. One time dose de-escalation to 22.5 mg subcutaneous injection due to intolerance or AEs was also allowed after the investigator carefully assessed the status of the subject.

Arm type	Experimental
Investigational medicinal product name	Product 1
Investigational medicinal product code	PF-00547659
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received PF-00547659 75 mg subcutaneous injection once in every 4 weeks through Week 72. One time dose escalation to 225 mg subcutaneous injection was allowed after 8 weeks of the study for the subjects who experienced clinical deterioration or unacceptably low level of response to study drug. One time dose de-escalation to 22.5 mg subcutaneous injection due to intolerance or AEs was also allowed after the investigator carefully assessed the status of the subject.

Number of subjects in period 1	PF-00547659 75 mg
Started	268
Completed	149
Not completed	119
Adverse event, serious fatal	2
Withdrawn Due to Pregnancy	1
Consent withdrawn by subject	47
Insufficient Clinical Response	22
Unspecified	7

Lost to follow-up	12
Adverse Event (Related to Study Drug)	8
Adverse Event(Not Related to Study Drug)	18
Protocol deviation	2

Baseline characteristics

Reporting groups	
Reporting group title	PF-00547659 75 mg

Reporting group description:

Subjects received PF-00547659 75 mg subcutaneous injection once in every 4 weeks through Week 72. One time dose escalation to 225 mg subcutaneous injection was allowed after 8 weeks of the study for the subjects who experienced clinical deterioration or unacceptably low level of response to study drug. One time dose de-escalation to 22.5 mg subcutaneous injection due to intolerance or AEs was also allowed after the investigator carefully assessed the status of the subject.

Reporting group values	PF-00547659 75 mg	Total	
Number of subjects	268	268	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 36.5 ± 11.7	 -	
Gender categorical Units: Subjects			
Female	151	151	
Male	117	117	

End points

End points reporting groups

Reporting group title	PF-00547659 75 mg

Reporting group description:

Subjects received PF-00547659 75 mg subcutaneous injection once in every 4 weeks through Week 72. One time dose escalation to 225 mg subcutaneous injection was allowed after 8 weeks of the study for the subjects who experienced clinical deterioration or unacceptably low level of response to study drug. One time dose de-escalation to 22.5 mg subcutaneous injection due to intolerance or AEs was also allowed after the investigator carefully assessed the status of the subject.

Primary: Number of Subjects with On-Treatment Adverse Events (AEs), AEs Led to Withdrawal, and Serious Adverse Events (SAEs)

End point title	Number of Subjects with On-Treatment Adverse Events (AEs), AEs Led to Withdrawal, and Serious Adverse Events (SAEs)[1]

End point description:

AEs included adverse drug reactions, illnesses with onset during the study, exacerbation of previous illnesses, clinically significant changes in physical examination findings and abnormal objective test findings (electrocardiogram (ECG), laboratory). An SAE was defined as any AE at any dose that resulted in death; was life threatening (immediate risk of death); required in-subject hospitalization or prolongation of existing hospitalization; resulted in a persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions); or resulted in congenital anomaly/birth defect. The modified intent-to-treat (mITT) population included all enrolled subjects who received at least 1 dose of investigational product was analysed for this end point.

End point type	Primary

End point timeframe:

From start of study treatment up to Week 72 (Treatment Period)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	PF-00547659 75 mg			
Subject group type	Reporting group			
Number of subjects analysed	268			
Units: subject				
Subjects With AEs	249			
Subjects With AEs Led to Withdrawal	53			
Subjects With SAEs	80			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Positive Anti-Drug (PF-00547659) Antibodies

End point title	Number of Subjects with Positive Anti-Drug (PF-00547659) Antibodies

End point description:

Positive Anti-Drug Antibodies (ADA) result was defined as ADA titre value greater than or equal to (>=) 4.64 at at least one of the time points. The modified intent-to-treat (mITT) population included all

enrolled subjects who received at least 1 dose of investigational product was analysed for this end point.

End point type	Secondary

End point timeframe:

Baseline up to Week 96

End point values	PF-00547659 75 mg			
Subject group type	Reporting group			
Number of subjects analysed	268			
Units: subject				
Subjects	63			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Trough Concentrations of PF-00547659 Versus Time

End point title	Serum Trough Concentrations of PF-00547659 Versus Time

End point description:

Serum trough concentrations of PF-00547659 were analyzed using population Pharmacokinetic (PK) methodology. The PK population included all enrolled subjects who received at least 1 dose of investigational product and had data on at least 1 PK concentration was analysed for this end point. Here "n" represents the number of subjects evaluable for this end point.

End point type	Secondary

End point timeframe:

Week 4,8,12,16,20,24,28,32,36,40,44,48,52,56,60,64,68,72,76,80,84,88,92,96

End point values	PF-00547659 75 mg			
Subject group type	Reporting group			
Number of subjects analysed	260			
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Week 4 (n=226)	6673 (± 6634.2)			
Week 8 (n=222)	6064 (± 4455.3)			
Week 12 (n=201)	8040 (± 6293.1)			
Week 16 (n=188)	9563 (± 7285.4)			
Week 20 (n=186)	10400 (± 8438.6)			
Week 24 (n=172)	10450 (± 7934.6)			
Week 28 (n=162)	10780 (± 9211)			

Week 32 (n=165)	11920 (± 10675)			
Week 36 (n=164)	12460 (± 9717.1)			
Week 40 (n=152)	12570 (± 10077)			
Week 44 (n=149)	12960 (± 10999)			
Week 48 (n=148)	13170 (± 11108)			
Week 52 (n=144)	13560 (± 11388)			
Week 56 (n=134)	13930 (± 11191)			
Week 60 (n=131)	14130 (± 11095)			
Week 64 (n=127)	14360 (± 11290)			
Week 68 (n=120)	14990 (± 12883)			
Week 72 (n=114)	13910 (± 10554)			
Week 76 (n=173)	10520 (± 10082)			
Week 80 (n=170)	3555 (± 5339.8)			
Week 84 (n=149)	1129 (± 2634.7)			
Week 88 (n=145)	403.8 (± 1522.6)			
Week 92 (n=136)	154.2 (± 1001.9)			
Week 96 (n=145)	54.73 (± 487.07)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Start of Study Treatment up to Safety Follow up (Week 96)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	PF-00547659 75 mg

Reporting group description:

Subjects received PF-00547659 75 mg subcutaneous injection once in every 4 weeks through Week 72. One time dose escalation to 225 mg subcutaneous injection was allowed after 8 weeks of the study for the subjects who experienced clinical deterioration or unacceptably low level of response to study drug. One time dose de-escalation to 22.5 mg subcutaneous injection due to intolerance or AEs was also allowed after the investigator carefully assessed the status of the subject.

Serious adverse events	PF-00547659 75 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	118 / 268 (44.03%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metastatic neoplasm			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Renal cancer			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Benign breast lump removal			

subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	2 / 268 (0.75%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Female genital tract fistula			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Menorrhagia			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Perineal fistula			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			

subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Investigations			
Blood creatine phosphokinase mm increased			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Haematocrit decreased			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Anastomotic leak			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fracture			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal stoma complication			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	2 / 268 (0.75%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Postoperative ileus			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Stomal hernia			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper limb fracture			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound dehiscence			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 268 (0.75%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Intracranial venous sinus thrombosis			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Visual impairment			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal hernia obstructive			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	3 / 268 (1.12%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Anal fistula			
subjects affected / exposed	7 / 268 (2.61%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Anal stenosis			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis ulcerative			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Crohn's disease			

subjects affected / exposed	44 / 268 (16.42%)		
occurrences causally related to treatment / all	1 / 51		
deaths causally related to treatment / all	0 / 0		
Duodenitis			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Enterocutaneous fistula			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorder			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ileal stenosis			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	4 / 268 (1.49%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Intestinal fistula			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal haemorrhage			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			

subjects affected / exposed	2 / 268 (0.75%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Large intestinal obstruction				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Large intestinal stenosis				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Melaena				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	3 / 268 (1.12%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	4 / 268 (1.49%)			
occurrences causally related to treatment / all	0 / 11			
deaths causally related to treatment / all	0 / 0			
Vomiting				

subjects affected / exposed	3 / 268 (1.12%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis acute			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	2 / 268 (0.75%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatic cyst			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Pyoderma gangrenosum			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Bladder dysfunction			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	2 / 268 (0.75%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Ureterolithiasis				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinoma				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Adrenocortical insufficiency acute				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arthritis				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arthritis enteropathic				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Muscle spasms				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Spinal column stenosis				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal osteoarthritis				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abdominal abscess				
subjects affected / exposed	2 / 268 (0.75%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Abdominal wall abscess				
subjects affected / exposed	2 / 268 (0.75%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Abscess intestinal				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abscess neck				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	10 / 268 (3.73%)			
occurrences causally related to treatment / all	1 / 10			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile infection				
subjects affected / exposed	3 / 268 (1.12%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Device related infection				

subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	3 / 268 (1.12%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Liver abscess				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pelvic abscess				
subjects affected / exposed	2 / 268 (0.75%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Perirectal abscess				
subjects affected / exposed	1 / 268 (0.37%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	3 / 268 (1.12%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	4 / 268 (1.49%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Postoperative abscess				

subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rotavirus infection			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Splenic abscess			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vulval abscess			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Fluid retention			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	PF-00547659 75 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	206 / 268 (76.87%)		
Nervous system disorders			
Headache			
subjects affected / exposed	35 / 268 (13.06%)		
occurrences (all)	45		
General disorders and administration			

site conditions			
Asthenia			
subjects affected / exposed	15 / 268 (5.60%)		
occurrences (all)	20		
Fatigue			
subjects affected / exposed	20 / 268 (7.46%)		
occurrences (all)	23		
Pyrexia			
subjects affected / exposed	27 / 268 (10.07%)		
occurrences (all)	36		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	49 / 268 (18.28%)		
occurrences (all)	59		
Anal fissure			
subjects affected / exposed	14 / 268 (5.22%)		
occurrences (all)	14		
Aphthous ulcer			
subjects affected / exposed	14 / 268 (5.22%)		
occurrences (all)	18		
Crohn's disease			
subjects affected / exposed	79 / 268 (29.48%)		
occurrences (all)	111		
Diarrhoea			
subjects affected / exposed	24 / 268 (8.96%)		
occurrences (all)	38		
Nausea			
subjects affected / exposed	32 / 268 (11.94%)		
occurrences (all)	44		
Vomiting			
subjects affected / exposed	23 / 268 (8.58%)		
occurrences (all)	34		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	83 / 268 (30.97%)		
occurrences (all)	113		

Back pain			
subjects affected / exposed	28 / 268 (10.45%)		
occurrences (all)	30		
Infections and infestations			
Anal abscess			
subjects affected / exposed	14 / 268 (5.22%)		
occurrences (all)	16		
Bronchitis			
subjects affected / exposed	20 / 268 (7.46%)		
occurrences (all)	26		
Gastroenteritis			
subjects affected / exposed	19 / 268 (7.09%)		
occurrences (all)	22		
Influenza			
subjects affected / exposed	18 / 268 (6.72%)		
occurrences (all)	19		
Nasopharyngitis			
subjects affected / exposed	54 / 268 (20.15%)		
occurrences (all)	93		
Pharyngitis			
subjects affected / exposed	15 / 268 (5.60%)		
occurrences (all)	18		
Upper respiratory tract infection			
subjects affected / exposed	20 / 268 (7.46%)		
occurrences (all)	25		
Urinary tract infection			
subjects affected / exposed	19 / 268 (7.09%)		
occurrences (all)	28		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 February 2011	Subjects were required to discontinue concomitant immunosuppressants prior to entering the open-label extension (OLE) study; interim analysis was added to study with statistical analysis modified accordingly.
17 May 2011	Included addition of footnotes to the Schedule of Activities to clarify which procedures would be carried forward from A7281006 (2010-023437-30) and A7281008 (2011-001443-74) Week 12 and not repeated. Addition of risk-benefit section; creation of section on Dosing to better describe the dose escalation and dose discontinuation criteria; update to reporting period for AEs; update of injection site monitoring instructions.
18 July 2011	Title of study updated; clarification to baseline procedures section and also other study visits in the Study Procedures section to specify that repeat NTproBNP, echocardiogram, and cardiology consultation should be performed for specified elevations in NTproBNP and that data were to be reviewed if applicable.
23 April 2012	Updates to protocol summary, study design, study design schematic, early withdrawal from OLE treatment for responders that relapse, minor administrative changes/corrections.
25 June 2012	Addition of Schedule of Activities for subjects enrolled in Japan and estimation of PK parameters for subjects enrolled in Japan.
01 August 2012	Addition of Appendix 8: Appendix 8 consisted of a version of the protocol to be implemented in Japan to accommodate specific requirements from the Pharmaceuticals and Medical Devices Agency.
19 February 2013	Revision of interim analysis section for clarification and revisions to PK analysis section and exploratory pharmacodynamics analysis section; revision to Data Monitoring Committee to indicate that the interim analysis results would be reviewed by the Data Monitoring Committee; added units from International System of Units for NTproBNP levels; addition of Simple Endoscopic Score for Crohn’s Disease (SES-CD).
09 December 2015	Removal of 18-month telephone call follow-up period and corresponding updates to protocol sections where applicable; addition of note for clarification of baseline for neurological assessments where applicable; and updates where applicable to be consistent with Pfizer standards.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported