



Clinical trial results:

A Phase 2a, Multicenter, Single Arm, Open-Label, Two-Stage, Study to Evaluate the Efficacy, Safety, Tolerability and Pharmacokinetics of PF-06480605 in Subjects With Moderate to Severe Ulcerative Colitis

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2016-001158-16 |
| Trial protocol | BE PL NL IT |
| Global end of trial date | 22 August 2018 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 |
| This version publication date | 18 July 2019 |
| First version publication date | 18 July 2019 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | B7541002 |
|-----------------------|----------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Pfizer, Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017 |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 30 November 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 31 May 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 22 August 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the safety and tolerability of PF-06480605 in subjects with moderate to severe ulcerative colitis, and to evaluate the efficacy of PF-06480605 in induction of endoscopic improvement (as assessed by Mayo endoscopic subscore) at Week 14 in subjects with moderate to severe ulcerative colitis.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 26 October 2016 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 3 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Belgium: 2 |
| Country: Number of subjects enrolled | Italy: 14 |
| Country: Number of subjects enrolled | Korea, Republic of: 1 |
| Country: Number of subjects enrolled | Netherlands: 1 |
| Country: Number of subjects enrolled | Poland: 22 |
| Country: Number of subjects enrolled | United States: 10 |
| Worldwide total number of subjects | 50 |
| EEA total number of subjects | 39 |

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) | 48 |
| From 65 to 84 years | 2 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 70 potential subjects were screened, and 50 of them were enrolled into the study.

Period 1

| | |
|------------------------------|------------------|
| Period 1 title | Treatment Period |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------|-----------------------|
| Arm title | PF-06480605 500 mg IV |
|------------------|-----------------------|

Arm description:

Subjects received PF-06480605 500 mg intravenously once every 2 weeks (Q2W) for a total of 7 doses (i.e., 12-week treatment period), and then were followed up for additional 14 weeks after the last dose of PF-06480605.

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | PF-06480605 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

PF-06480605 500 mg was administered intravenously every 2 weeks for a total of 7 doses.

| | |
|---------------------------------------|-----------------------|
| Number of subjects in period 1 | PF-06480605 500 mg IV |
| Started | 50 |
| Completed | 49 |
| Not completed | 1 |
| Adverse event, non-fatal | 1 |

Period 2

| | |
|------------------------------|----------------|
| Period 2 title | Follow-Up |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|--|-----------------------------------|
| Arm title | PF-06480605 500 mg IV |
| Arm description: | |
| Subjects received PF-06480605 500 mg intravenously once every 2 weeks (Q2W) for a total of 7 doses (i.e., 12-week treatment period), and then were followed up for additional 14 weeks after the last dose of PF-06480605. | |
| Arm type | Experimental |
| Investigational medicinal product name | PF-06480605 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

PF-06480605 500 mg was administered intravenously every 2 weeks for a total of 7 doses.

| | |
|---------------------------------------|-----------------------|
| Number of subjects in period 2 | PF-06480605 500 mg IV |
| Started | 49 |
| Completed | 42 |
| Not completed | 7 |
| Withdrawal of Consent | 2 |
| Consent withdrawn by subject | 4 |
| Lack of efficacy | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------------------|
| Reporting group title | PF-06480605 500 mg IV |
|-----------------------|-----------------------|

Reporting group description:

Subjects received PF-06480605 500 mg intravenously once every 2 weeks (Q2W) for a total of 7 doses (i.e., 12-week treatment period), and then were followed up for additional 14 weeks after the last dose of PF-06480605.

| Reporting group values | PF-06480605 500 mg IV | Total | |
|--|-----------------------|-------|--|
| Number of subjects | 50 | 50 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 48 | 48 | |
| From 65-84 years | 2 | 2 | |
| 85 years and over | 0 | 0 | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 40.0 | | |
| standard deviation | ± 14.52 | - | |
| Sex: Female, Male | | | |
| Units: Subjects | | | |
| Female | 22 | 22 | |
| Male | 28 | 28 | |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| White | 48 | 48 | |
| Asian | 2 | 2 | |

End points

End points reporting groups

| | |
|--|-----------------------|
| Reporting group title | PF-06480605 500 mg IV |
| Reporting group description: Subjects received PF-06480605 500 mg intravenously once every 2 weeks (Q2W) for a total of 7 doses (i.e., 12-week treatment period), and then were followed up for additional 14 weeks after the last dose of PF-06480605. | |
| Reporting group title | PF-06480605 500 mg IV |
| Reporting group description: Subjects received PF-06480605 500 mg intravenously once every 2 weeks (Q2W) for a total of 7 doses (i.e., 12-week treatment period), and then were followed up for additional 14 weeks after the last dose of PF-06480605. | |

Primary: Number of Subjects with Treatment-Emergent Adverse Events, Serious Adverse Events, and Who Withdrew Due to Adverse Events

| | |
|---|--|
| End point title | Number of Subjects with Treatment-Emergent Adverse Events, Serious Adverse Events, and Who Withdrew Due to Adverse Events ^[1] |
| End point description: An adverse event (AE) was defined as any untoward medical occurrence in a clinical investigation subject administered a product or medical device; the event need not necessarily have a causal relationship with the treatment or usage. A serious AE (SAE) was any untoward medical occurrence at any dose that (1) resulted in death; (2) was life-threatening (immediate risk of death); (3) required inpatient hospitalization or prolongation of existing hospitalization; (4) resulted in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions); (5) resulted in congenital anomaly/birth defect. A treatment-emergent AE (TEAE) was defined as an event that emerged during treatment having been absent pre-treatment, or worsened relative to the pre-treatment state. Causality to study treatment was determined by the investigator. The analysis population included all subjects who received at least 1 dose of PF-06480605. | |
| End point type | Primary |
| End point timeframe: Day 1 up to final onsite visit (Week 26) | |

Notes:

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

Justification: No statistical analysis was performed for this endpoint

| | | | | |
|-----------------------------|-----------------------|--|--|--|
| End point values | PF-06480605 500 mg IV | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 50 | | | |
| Units: subjects | | | | |
| All-causality AEs | 33 | | | |
| All-causality SAEs | 3 | | | |
| Treatment-related AEs | 8 | | | |
| Treatment-related SAEs | 1 | | | |
| Withdrew due to AEs | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Laboratory Abnormalities

| | |
|-----------------|---|
| End point title | Number of Subjects with Laboratory Abnormalities ^[2] |
|-----------------|---|

End point description:

The following parameters were evaluated: hematology (hemoglobin, hematocrit, erythrocytes, erythrocyte mean corpuscular volume, platelets, leukocytes, lymphocytes, neutrophils, basophils, eosinophils, monocytes, activated partial thromboplastin time, and prothrombin time), clinical chemistry (bilirubin, direct bilirubin, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, protein, albumin, blood urea nitrogen, creatinine, urate, sodium, potassium, chloride, calcium, glucose, and creatine kinase), and urinalysis (urine glucose, ketones, urine protein, urine hemoglobin, nitrite, leukocyte esterase, urine erythrocytes, urine leukocytes, hyaline casts, and bacteria). The analysis population included all subjects who received at least 1 dose of PF-06480605.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 1 up to final onsite visit (Week 26)

Notes:

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

Justification: No statistical analysis was performed for this endpoint

| | | | | |
|-----------------------------|--------------------------|--|--|--|
| End point values | PF-06480605 500 mg IV | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 50 | | | |
| Units: subjects | 38 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Vital Signs Data Meeting Pre-specified Criteria

| | |
|-----------------|--|
| End point title | Number of Subjects with Vital Signs Data Meeting Pre-specified Criteria ^[3] |
|-----------------|--|

End point description:

Vital signs evaluation included sitting diastolic blood pressure (DBP), systolic blood pressure (SBP), and pulse rate. Sitting blood pressure was measured with the subject's arm supported at the level of the heart, and recorded to the nearest millimeters of mercury (mm Hg). The same size BP cuff which had been properly sized and calibrated was used to measure BP each time. Number of subjects with vital signs data meeting pre-specified criteria is presented. The analysis population included all subjects who received at least 1 dose of PF-06480605.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline up to final onsite visit (Week 26)

Notes:

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

Justification: No statistical analysis was performed for this endpoint

| | | | | |
|--|--------------------------|--|--|--|
| End point values | PF-06480605 500 mg IV | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 50 | | | |
| Units: subjects | | | | |
| Sitting DBP <50 mm Hg | 1 | | | |
| Sitting SBP <90 mm Hg | 4 | | | |
| Sitting pulse rate <40 beats per minute (bpm) | 0 | | | |
| Sitting pulse rate >120 bpm | 1 | | | |
| Sitting DBP increase from baseline >=20 mm Hg | 2 | | | |
| Sitting SBP increase from baseline >=30 mm Hg | 5 | | | |
| Sitting DBP decrease from baseline >=20 mm Hg | 7 | | | |
| Sitting SBP decrease from baseline >=30 mm Hg | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Electrocardiogram (ECG) Data Meeting Pre-specified Criteria

| | |
|-----------------|--|
| End point title | Number of Subjects with Electrocardiogram (ECG) Data Meeting Pre-specified Criteria ^[4] |
|-----------------|--|

End point description:

All scheduled 12-lead ECGs were performed after the subject had rested quietly for at least 10 minutes in a supine position. Number of subjects with ECG data meeting pre-specified criteria is presented. The analysis population included all subjects who received at least 1 dose of PF-06480605 and had both baseline and at least 1 post-baseline ECG evaluation performed.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline up to final onsite visit (Week 26)

Notes:

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

Justification: No statistical analysis was performed for this endpoint

| | | | | |
|---|--------------------------|--|--|--|
| End point values | PF-06480605 500 mg IV | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 49 | | | |
| Units: subjects | | | | |
| PR interval >=300 milliseconds (msec) | 0 | | | |
| QRS duration >=140 msec | 0 | | | |
| QT interval >=500 msec | 0 | | | |
| QTcF interval: 450 to <480 msec | 5 | | | |
| QTcF interval: 480 to <500 msec | 0 | | | |
| QTcF interval: >=500 msec | 0 | | | |
| PR interval increase from baseline >=25%/50% | 0 | | | |

| | | | | |
|--|---|--|--|--|
| QRS duration increase from baseline ≥50% | 0 | | | |
| QTcF increase from baseline: 30 to <60 msec | 9 | | | |
| QTcF increase from baseline: ≥60 msec | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Achieving Endoscopic Improvement at Week 14, Based on Uniformly Minimum-Variance Unbiased Estimator (UMVUE) - Per Protocol Analysis Set

| | |
|-----------------|---|
| End point title | Percentage of Subjects Achieving Endoscopic Improvement at Week 14, Based on Uniformly Minimum-Variance Unbiased Estimator (UMVUE) - Per Protocol Analysis Set ^[5] |
|-----------------|---|

End point description:

Endoscopic improvement at Week 14 was defined as Mayo endoscopic sub-score of 0 or 1, and without friability. The Mayo scoring system was used to assess ulcerative colitis activity, and it ranges from 0 to 12, calculated as sum of 4 sub-scores, with higher scores indicating more severe disease. The 4 sub-scores are stool frequency (0=normal number of stools; 1=1 to 2 stools more than normal; 2=3 to 4 stools more than normal; 3=5 or more stools more than normal); rectal bleeding (0=no blood seen; 1=streaks of blood with stools less than half the time; 2=obvious blood with stool most of the time; 3=blood alone passes); findings on endoscopy (0=normal or inactive disease; 1=mild disease [erythema, decreased vascular pattern, mild friability]; 2=moderate disease [marked erythema, lack of vascular pattern, friability, erosions]; 3=severe disease [spontaneous bleeding, ulceration]); and physician's global assessment (0=normal; 1=mild disease; 2=moderate disease; 3=severe disease).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Week 14

Notes:

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

Justification: No statistical analysis was performed for this endpoint

| | | | | |
|----------------------------------|---------------------------|--|--|--|
| End point values | PF-06480605 500 mg IV | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 45 | | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 38.20 (23.82 to 53.68) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Remission at Week 14 – Full Analysis Set

| | |
|-----------------|---|
| End point title | Percentage of Subjects Achieving Remission at Week 14 – Full Analysis Set |
|-----------------|---|

End point description:

Remission: total Mayo score ≤ 2 with no individual subscore > 1 . Mayo scoring system was used to assess ulcerative colitis activity (range: 0 to 12, calculated as sum of 4 subscores, higher scores indicating more severe disease). The 4 subscores are stool frequency (0=normal number of stools; 1=1 to 2 stools more than normal; 2=3 to 4 stools more than normal; 3=5 or more stools more than normal); rectal bleeding (0=no blood seen; 1=streaks of blood with stools less than half the time; 2=obvious blood with stool most of the time; 3=blood alone passes); findings on modified endoscopy (0=normal or inactive disease; 1=mild disease [erythema, decreased vascular pattern, no friability]; 2=moderate disease [marked erythema, lack of vascular pattern, friability, erosions]; 3=severe disease [spontaneous bleeding, ulceration]); and physician's global assessment (0=normal; 1=mild disease; 2=moderate disease; 3=severe disease).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 14

| | | | | |
|----------------------------------|---------------------------|--|--|--|
| End point values | PF-06480605 500 mg IV | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 50 | | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 24.00 (13.06 to 38.17) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Remission at Week 14 – Per Protocol Analysis Set

| | |
|-----------------|---|
| End point title | Percentage of Subjects Achieving Remission at Week 14 – Per Protocol Analysis Set |
|-----------------|---|

End point description:

Remission: total Mayo score ≤ 2 with no individual subscore > 1 . Mayo scoring system was used to assess ulcerative colitis activity (range: 0 to 12, calculated as sum of 4 subscores, higher scores indicating more severe disease). The 4 subscores are stool frequency (0=normal number of stools; 1=1 to 2 stools more than normal; 2=3 to 4 stools more than normal; 3= 5 or more stools more than normal); rectal bleeding (0=no blood seen; 1=streaks of blood with stools less than half the time; 2=obvious blood with stool most of the time; 3=blood alone passes); findings on modified endoscopy (0=normal or inactive disease; 1=mild disease [erythema, decreased vascular pattern, no friability]; 2=moderate disease [marked erythema, lack of vascular pattern, friability, erosions]; 3=severe disease [spontaneous bleeding, ulceration]); and physician's global assessment (0=normal; 1=mild disease; 2=moderate disease; 3=severe disease).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 14

| | | | | |
|----------------------------------|---------------------------|--|--|--|
| End point values | PF-06480605 500 mg IV | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 45 | | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 26.67 (14.60 to 41.94) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Endoscopic Remission at Week 14 - Full Analysis Set

| | |
|--|--|
| End point title | Percentage of Subjects Achieving Endoscopic Remission at Week 14 - Full Analysis Set |
| End point description: | |
| Endoscopic remission at Week 14 was defined as Mayo endoscopic sub-score of 0. The Mayo scoring system was used to assess ulcerative colitis activity, and it ranges from 0 to 12, calculated as sum of 4 sub-scores, with higher scores indicating more severe disease. The 4 sub-scores are stool frequency (0=normal number of stools; 1=1 to 2 stools more than normal; 2= 3 to 4 stools more than normal; 3= 5 or more stools more than normal); rectal bleeding (0=no blood seen; 1=streaks of blood with stools less than half the time; 2=obvious blood with stool most of the time; 3=blood alone passes); findings on endoscopy (0=normal or inactive disease; 1=mild disease [erythema, decreased vascular pattern, mild friability]; 2=moderate disease [marked erythema, lack of vascular pattern, friability, erosions]; 3=severe disease [spontaneous bleeding, ulceration]); and physician's global assessment (0=normal; 1=mild disease; 2=moderate disease; 3=severe disease). | |
| End point type | Secondary |
| End point timeframe: | |
| Week 14 | |

| | | | | |
|----------------------------------|--------------------------|--|--|--|
| End point values | PF-06480605 500 mg IV | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 50 | | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 10.00 (3.33 to 21.81) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Serum Concentration (Cmax) of PF-06480605

| | |
|--|---|
| End point title | Maximum Serum Concentration (Cmax) of PF-06480605 |
| End point description: | |
| Maximum serum concentration (Cmax) of PF-06480605 was observed directly from data. The analysis population included all enrolled subjects who received at least 1 dose of PF-06480605 and in whom at least 1 concentration value | |

was reported.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 30 minutes pre-dose and 1 hour post-dose on Day 85 | |

| | | | | |
|---|--------------------------|--|--|--|
| End point values | PF-06480605 500 mg IV | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 44 | | | |
| Units: nanograms (ng)/milliliters (mL) | | | | |
| geometric mean (geometric coefficient of variation) | 263400 (\pm 54) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Average Serum Concentration (Cav) of PF-06480605

| | |
|---|--|
| End point title | Average Serum Concentration (Cav) of PF-06480605 |
| End point description: | |
| Average serum concentration (Cav) of PF-06480605 was calculated as AUCtau/tau, where tau was the dosing interval (tau=14 days), and AUCtau was the area under the concentration-time profile from time 0 to time tau. The analysis population included all enrolled subjects who received at least 1 dose of PF-06480605 and had at least 1 derived value of a specific pharmacokinetic (PK) parameter. | |
| End point type | Secondary |
| End point timeframe: | |
| 30 minutes pre-dose and 1 hour post-dose on Day 85 | |

| | | | | |
|---|--------------------------|--|--|--|
| End point values | PF-06480605 500 mg IV | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 44 | | | |
| Units: nanograms (ng)/milliliters (mL) | | | | |
| geometric mean (geometric coefficient of variation) | 171400 (\pm 45) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Lowest Serum Concentration (Cmin) of PF-06480605

| | |
|-----------------|--|
| End point title | Lowest Serum Concentration (Cmin) of PF-06480605 |
|-----------------|--|

End point description:

Lowest serum concentration (C_{min}) of PF-06480605 was observed directly from data. The analysis population included all enrolled subjects who received at least 1 dose of PF-06480605 and in whom at least 1 concentration value was reported.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

30 minutes pre-dose and 1 hour post-dose on Day 85

| | | | | |
|---|--------------------------|--|--|--|
| End point values | PF-06480605 500 mg IV | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 44 | | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | 87650 (± 50) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the Concentration-time Profile from Time Zero to Time Tau (AUC_{tau}) of PF-06480605

| | |
|-----------------|---|
| End point title | Area under the Concentration-time Profile from Time Zero to Time Tau (AUC _{tau}) of PF-06480605 |
|-----------------|---|

End point description:

AUC_{tau} of PF-06480605 was calculated using linear/log trapezoidal method; tau was the dosing interval (=14 days). The analysis population included all enrolled subjects who received at least 1 dose of PF-06480605 and had at least 1 derived value of a specific pharmacokinetic (PK) parameter.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

30 minutes pre-dose and 1 hour post-dose on Day 85

| | | | | |
|---|--------------------------|--|--|--|
| End point values | PF-06480605 500 mg IV | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 45 | | | |
| Units: ng.hr/mL | | | | |
| geometric mean (geometric coefficient of variation) | 57610000 (± 45) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Developed Anti-drug Antibodies (ADAs) and Neutralizing Antibodies (NABs)

| | |
|-----------------|---|
| End point title | Percentage of Subjects Who Developed Anti-drug Antibodies (ADAs) and Neutralizing Antibodies (NABs) |
|-----------------|---|

End point description:

Serum samples were analyzed using a new ADA assay with acid pre-treatment followed by a more drug-tolerant cell-based NAb assay. For ADA assay with acid pre-treatment, the sample was deemed positive if log titer ≥ 1.30 ; for cell-based NAb assay, the sample was deemed positive if log titer ≥ 0.699 . The analysis population included all enrolled subjects who received at least 1 dose of PF-06480605 with at least 1 post-treatment ADA determination.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 1 up to final onsite visit (Week 26)

| | | | | |
|-------------------------------|--------------------------|--|--|--|
| End point values | PF-06480605 500 mg IV | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 50 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| ADA | 82.0 | | | |
| NAb | 10.0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Fecal Calprotectin

| | |
|-----------------|--|
| End point title | Change from Baseline in Fecal Calprotectin |
|-----------------|--|

End point description:

Fecal calprotectin has been used to detect intestinal inflammation (colitis or enteritis) and can serve as a biomarker for inflammatory bowel diseases. Elevated fecal calprotectin levels indicate migration of neutrophils into the intestinal mucosa, which occurs during intestinal inflammation.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 2, 8, 12 and 26

| | | | | |
|--------------------------------------|-------------------------------|--|--|--|
| End point values | PF-06480605 500 mg IV | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 48 | | | |
| Units: micrograms/grams | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 3662.25 (\pm 3556.331) | | | |
| Week 2 change from baseline | -1861.38 (\pm 3565.861) | | | |

| | | | | |
|------------------------------|----------------------------|--|--|--|
| Week 8 change from baseline | -2509.43 (\pm 3751.843) | | | |
| Week 12 change from baseline | -2844.26 (\pm 3623.922) | | | |
| Week 26 change from baseline | -2726.97 (\pm 3673.063) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in High Sensitivity C-reactive Protein (HsCRP)

| | |
|-----------------|---|
| End point title | Change from Baseline in High Sensitivity C-reactive Protein (HsCRP) |
|-----------------|---|

End point description:

HsCRP is used mainly as a marker of inflammation. The analysis population included all subjects who received at least 1 dose of PF 06480605 with 1 hsCRP measurement.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 2, 4, 6, 8, 10, 12, 14, 16, 20, 24, and 26

| | | | | |
|--------------------------------------|--------------------------|--|--|--|
| End point values | PF-06480605 500 mg IV | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 48 | | | |
| Units: micrograms/deciliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 0.9316 (\pm 1.15545) | | | |
| Week 2 change from baseline | -0.2136 (\pm 1.43785) | | | |
| Week 4 change from baseline | -0.4883 (\pm 1.10820) | | | |
| Week 6 change from baseline | -0.3314 (\pm 1.39605) | | | |
| Week 8 change from baseline | -0.4875 (\pm 1.00870) | | | |
| Week 10 change from baseline | -0.5738 (\pm 0.97608) | | | |
| Week 12 change from baseline | -0.4242 (\pm 1.18416) | | | |
| Week 14 change from baseline | -0.3983 (\pm 1.21181) | | | |
| Week 16 change from baseline | -0.5070 (\pm 1.37798) | | | |
| Week 20 change from baseline | -0.4728 (\pm 1.11950) | | | |
| Week 24 change from baseline | -0.5334 (\pm 1.03224) | | | |
| Week 26 change from baseline | -0.3453 (\pm 1.37576) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Serum Total Soluble Tumor Necrosis Factor-like Ligand 1A (sTL1A)

| | |
|-----------------|--|
| End point title | Change from Baseline in Serum Total Soluble Tumor Necrosis Factor-like Ligand 1A (sTL1A) |
|-----------------|--|

End point description:

TL1A is a member of the tumor necrosis factor (TNF) family of cytokines. The investigational product of this study PF-06480605 is a fully human neutralizing antibody against TL1A. The analysis population included all subjects who received at least 1 dose of PF 06480605 with 1 sTL1A measurement.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 2, 4, 6, 8, 10, 12, 14, 16, 20, 24, and 26

| End point values | PF-06480605 500 mg IV | | | |
|--------------------------------------|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 49 | | | |
| Units: picograms/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 118.9 (± 36.67) | | | |
| Week 2 change from baseline | 3845.0 (± 1552.33) | | | |
| Week 4 change from baseline | 6114.1 (± 2428.38) | | | |
| Week 6 change from baseline | 7793.5 (± 3802.53) | | | |
| Week 8 change from baseline | 8267.5 (± 4133.73) | | | |
| Week 10 change from baseline | 8149.5 (± 4761.70) | | | |
| Week 12 change from baseline | 7354.0 (± 5070.54) | | | |
| Week 14 change from baseline | 7201.2 (± 5576.76) | | | |
| Week 16 change from baseline | 5969.5 (± 5632.95) | | | |
| Week 20 change from baseline | 4141.7 (± 4547.17) | | | |
| Week 24 change from baseline | 3518.4 (± 3534.65) | | | |
| Week 26 change from baseline | 3448.7 (± 3369.80) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to final onsite visit (Week 26)

Adverse event reporting additional description:

The same event may appear as both a non-serious adverse event and a serious adverse event. 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 | 21.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------|
| Reporting group title | PF-06480605 500 mg IV |
|-----------------------|-----------------------|

Reporting group description:

Subjects received PF-06480605 500 mg intravenously once every 2 weeks (Q2W) for a total of 7 doses (i.e., 12-week treatment period), and then were followed up for additional 14 weeks after the last dose of PF-06480605.

| Serious adverse events | PF-06480605 500 mg IV | | |
|---|-----------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Gastrointestinal disorders | | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Peritonitis | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| 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-06480605 500 mg IV | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 20 / 50 (40.00%) | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 3 | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 5 / 50 (10.00%) | | |
| occurrences (all) | 5 | | |
| Nausea | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 7 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 6 / 50 (12.00%) | | |
| occurrences (all) | 6 | | |
| Back pain | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 3 | | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 3 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 3 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 18 May 2016 | Revisions were made on Schedule of Activities, objectives/endpoints, inclusion and exclusion criteria, etc. |
| 12 January 2017 | Revisions were made on Schedule of Activities, objectives/endpoints, inclusion and exclusion criteria, etc. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported