# Clinical trial results:
# A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Multi-Center Study to Evaluate the Efficacy and Safety of Once-Daily Administration of a Chemokine CCR2/5 Receptor Antagonist (PF-04634817) in Adults With Type 2 Diabetes and Overt Nephropathy

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

## Summary

| | |
|---|---|
| EudraCT number | 2012-003332-23 |
| Trial protocol | IT DE ES PL RO |
| Global end of trial date | 22 September 2014 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 29 July 2016 |
| First version publication date | 29 July 2016 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | B1261007 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01712061 |
| 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, Inc., Pfizer ClinicalTrials.gov Call Center, 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 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 | 01 September 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 22 September 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 22 September 2014 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the efficacy of PF-04634817 compared to placebo in the reduction of albuminuria following 12 weeks of treatment in subjects with Type 2 diabetes and overt nephropathy.

Protection of trial subjects:

This study used an unblinded Internal Review Committee (IRC) for the interim analysis.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 13 December 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Argentina: 6 |
| Country: Number of subjects enrolled | Australia: 14 |
| Country: Number of subjects enrolled | Germany: 12 |
| Country: Number of subjects enrolled | Hong Kong: 3 |
| Country: Number of subjects enrolled | Italy: 8 |
| Country: Number of subjects enrolled | Canada: 23 |
| Country: Number of subjects enrolled | Korea, Republic of: 9 |
| Country: Number of subjects enrolled | Malaysia: 5 |
| Country: Number of subjects enrolled | Peru: 10 |
| Country: Number of subjects enrolled | Poland: 8 |
| Country: Number of subjects enrolled | Romania: 11 |
| Country: Number of subjects enrolled | United States: 107 |
| Country: Number of subjects enrolled | Spain: 10 |
| Worldwide total number of subjects | 226 |
| EEA total number of subjects | 49 |

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) | 112 |
| From 65 to 84 years | 114 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The primary entry criterion for participants was based on presence of macroalbuminuria (urine albumin to creatinine ratio [UACR] greater than or equal to (>=)300 milligrams per gram (mg/g).

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | No |
| **Arm title** | PF-04634817 150 mg Daily |

Arm description:

Subjects with estimated glomerular filtration rate (eGFR) values of 20 to less than (<)30 milliliters/minute (mL/min)/1.73 square meter (m^2) were dosed orally at 150 mg once daily for 12 weeks.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | PF-04634817 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

150 mg

| | |
|---|---|
| **Arm title** | PF-04634817 200 mg Daily |

Arm description:

Subjects with eGFR values of 30 to 75 mL/min/1.73 m^2 were dosed orally at 200 mg once daily for 12 weeks.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | PF-04634817 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

200 mg

| | |
|---|---|
| **Arm title** | PF-04634817 200 mg/150 mg Daily |

Arm description:

Subjects received either 150 mg or 200 mg once daily for 12 weeks.

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | PF-04634817 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

150 mg or 200 mg once daily

| | |
|---|---|
| **Arm title** | Placebo Daily |

Arm description:

Subjects were dosed orally with matching placebo tablets once daily for 12 weeks.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

placebo matched PF-04634817

| **Number of subjects in period 1** | PF-04634817 150 mg Daily | PF-04634817 200 mg Daily | PF-04634817 200 mg/150 mg Daily |
|---|---|---|---|
| Started | 30 | 140 | 170 |
| Completed | 20 | 114 | 134 |
| Not completed | 10 | 26 | 36 |
| Adverse event, serious fatal | - | - | - |
| Consent withdrawn by subject | 1 | 7 | 8 |
| Did Not Meet Entrance Criteria | 4 | 6 | 10 |
| Adverse event, non-fatal | 4 | 9 | 13 |
| Medication Error Without Associated AE | - | 1 | 1 |
| Unspecified | - | 3 | 3 |
| Lost to follow-up | 1 | - | 1 |

| **Number of subjects in period 1** | Placebo Daily |
|---|---|
| Started | 56 |
| Completed | 45 |
| Not completed | 11 |
| Adverse event, serious fatal | 1 |
| Consent withdrawn by subject | 1 |
| Did Not Meet Entrance Criteria | 3 |
| Adverse event, non-fatal | 5 |
| Medication Error Without Associated AE | - |
| Unspecified | - |
| Lost to follow-up | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Overall Study |

Reporting group description: -

| Reporting group values | Overall Study | Total | |
|---|---|---|---|
| Number of subjects | 226 | 226 | |
| Age categorical<br>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) | 112 | 112 | |
| From 65-84 years | 114 | 114 | |
| 85 years and over | 0 | 0 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 64.1 | | |
| standard deviation | ± 8.6 | - | |
| Gender, Male/Female<br>Units: Participants | | | |
| FEMALE | 43 | 43 | |
| MALE | 183 | 183 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | PF-04634817 150 mg Daily |
| Reporting group description: | |
| Subjects with estimated glomerular filtration rate (eGFR) values of 20 to less than (<)30 milliliters/minute (mL/min)/1.73 square meter (m^2) were dosed orally at 150 mg once daily for 12 weeks. | |
| Reporting group title | PF-04634817 200 mg Daily |
| Reporting group description: | |
| Subjects with eGFR values of 30 to 75 mL/min/1.73 m^2 were dosed orally at 200 mg once daily for 12 weeks. | |
| Reporting group title | PF-04634817 200 mg/150 mg Daily |
| Reporting group description: | |
| Subjects received either 150 mg or 200 mg once daily for 12 weeks. | |
| Reporting group title | Placebo Daily |
| Reporting group description: | |
| Subjects were dosed orally with matching placebo tablets once daily for 12 weeks. | |

### Primary: Percent Reduction From Baseline in Urinary Albumin to Creatinine Ratio (UACR) at Week 12

| | |
|---|---|
| End point title | Percent Reduction From Baseline in Urinary Albumin to Creatinine Ratio (UACR) at Week 12[1] |
| End point description: | |
| | |
| End point type | Primary |
| End point timeframe: | |
| Baseline and Week 12 | |

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: No statistical analysis was planned for this safety endpoint. Safety data were summarized using Sponsor Data Standards.

| End point values | PF-04634817 200 mg/150 mg Daily | Placebo Daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 159 | 51 | | |
| Units: percent (%) | | | | |
| arithmetic mean (confidence interval 95%) | 13.27 (3.14 to 24.62) | 5.02 (-7.9 to 18.7) | | |

### Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | Percent Reduction from Baseline in UACR at Week 12 |
| Comparison groups | PF-04634817 200 mg/150 mg Daily v Placebo Daily |

| | |
|---|---|
| Number of subjects included in analysis | 210 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Bayesian ANCOVA |
| Point estimate | 0.91785 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.75 |
| upper limit | 1.09 |

## Secondary: Change From Baseline in UACR at Weeks 4, 8 and 16

| | |
|---|---|
| End point title | Change From Baseline in UACR at Weeks 4, 8 and 16[2] |

End point description:

The presence of albumin in the urine (macroalbuminuria) is a marker of kidney disease. Albumin and creatinine concentrations were obtained from spot urine samples.

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

End point timeframe:

Baseline, Weeks 4, 8 and 16

Notes:

[2] - 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: No statistical analysis was planned for this secondary endpoint. Secondary analyses included tabulations of summary statistics of all continuous secondary endpoints.

| **End point values** | PF-04634817 200 mg/150 mg Daily | Placebo Daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 159 | 51 | | |
| Units: mg/millimolar creatinine (mmolCr) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Baseline (n=157,50) | 127.41 (± 96) | 121.8 (± 88) | | |
| Change From Baseline at Week 4 (n=148,46) | 0.89 (± 66) | 0.91 (± 88) | | |
| Change From Baseline at Week 8 (n=134,43) | 0.9 (± 62) | 0.94 (± 57) | | |
| Change From Baseline at Week 16 (n=126,37) | 0.93 (± 72) | 0.92 (± 56) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Urinary Protein to Creatinine Ratio (UPCR) at Weeks 4, 8, 12 and 16

| | |
|---|---|
| End point title | Change From Baseline in Urinary Protein to Creatinine Ratio (UPCR) at Weeks 4, 8, 12 and 16[3] |

End point description:

The presence of protein in the urine (proteinuria) often implies kidney disease. Protein and creatinine concentrations were obtained from spot urine samples.

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

End point timeframe:

Baseline, Weeks 4, 8, 12 and 16

Notes:

[3] - 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: No statistical analysis was planned for this secondary endpoint. Secondary analyses included tabulations of summary statistics of all continuous secondary endpoints.

| **End point values** | PF-04634817 200 mg/150 mg Daily | Placebo Daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 159 | 51 | | |
| Units: mg/mmolCr | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Baseline (n=155,49) | 185.42 (± 97) | 176.31 (± 82) | | |
| Change From Baseline at Week 4 (n=143,45) | 0.93 (± 47) | 0.92 (± 76) | | |
| Change From Baseline at Week 8 (n=130,42) | 0.92 (± 50) | 0.94 (± 46) | | |
| Change From Baseline at Week 12 (n=125,42) | 0.92 (± 58) | 0.92 (± 79) | | |
| Change From Baseline at Week 16 (n=125,36) | 0.95 (± 58) | 0.92 (± 55) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Estimated Glomerular Filtration Rate (eGFR) Using the Abbreviated Modified Diet in Renal Disease (MDRD) Formula at Weeks 1, 4, 8, 12 and 16

| End point title | Change From Baseline in Estimated Glomerular Filtration Rate (eGFR) Using the Abbreviated Modified Diet in Renal Disease (MDRD) Formula at Weeks 1, 4, 8, 12 and 16[4] |
|---|---|

End point description:

eGFR was calculated using the MDRD equation and normalized to 1.73 m^2 body surface area. Age and corresponding creatinine at each visit (Weeks 1, 4, 8, 12 and 16) were used to calculate GFR

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

End point timeframe:

Baseline, Week 1, 4, 8, 12 and 16

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The warning is not true, statistical analysis was reported for all the arms in the baseline period.

| End point values | PF-04634817 200 mg/150 mg Daily | Placebo Daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 159 | 51 | | |
| Units: mL/min/1.73m^2 | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=159,51) | 41.8 (± 12.18) | 41.65 (± 13.46) | | |
| Change From Baseline at Week 1 (n=157,50) | -0.77 (± 5.8) | -0.35 (± 5.28) | | |
| Change From Baseline at Week 4 (n=157,51) | -1.07 (± 5.37) | -1.32 (± 5.12) | | |
| Change From Baseline at Week 8 (n=147,47) | -1.6 (± 5.34) | -2.15 (± 6.83) | | |
| Change From Baseline at Week 12 (n=136,45) | -1.14 (± 5.7) | -1.03 (± 5.75) | | |
| Change From Baseline at Week 16 (n=134,44) | -2.14 (± 6.42) | -1.18 (± 5.58) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in eGFR Using Cystatin Formula at Weeks 12 and 16

| End point title | Change From Baseline in eGFR Using Cystatin Formula at Weeks 12 and 16[5] |
|---|---|

End point description:

Serum cystatin C may be a more reliable endogenous marker of GFR than serum creatinine. eGFR was calculated using the Cystatin Formula and normalized to 1.73 m^2 body surface area.

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

End point timeframe:

Baseline, Week 12, and Week 16

Notes:

[5] - 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: No statistical analysis was planned for this secondary endpoint. Secondary analyses included tabulations of summary statistics of all continuous secondary endpoints.

| End point values | PF-04634817 200 mg/150 mg Daily | Placebo Daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 159 | 51 | | |
| Units: mL/min/1.73m^2 | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=159,50) | 45.28 (± 14.22) | 45.36 (± 14.94) | | |
| Change From Baseline at Week 12 (n=135,44) | -1.1 (± 6.3) | -0.7 (± 5.49) | | |
| Change From Baseline at Week 16 (n=134,43) | -2.27 (± 6.77) | -0.91 (± 6.3) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Serum Creatinine at Weeks 1, 4, 8, 12 and 16

| End point title | Change From Baseline in Serum Creatinine at Weeks 1, 4, 8, 12 and 16[6] |
|---|---|

End point description:

Serum creatinine is an indicator of kidney function. Creatinine is a substance formed from the metabolism of creatine, commonly found in blood, urine, and muscle tissue. It is removed from the blood by the kidneys and excreted in urine. Normal adult blood levels of creatinine=45 to 90 micromoles per liter (mcmol/L) for females, 60 to 110 mcmol/L for males, however normal values are age-dependent. Change from baseline=creatinine level at Week 1, 4, 8, 12 or 16 minus baseline level where higher scores represented decreased kidney function.

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

End point timeframe:

Baseline, Week 1, 4, 8, 12 and 16

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this secondary endpoint. Secondary analyses included tabulations of summary statistics of all continuous secondary endpoints.

| **End point values** | PF-04634817 200 mg/150 mg Daily | Placebo Daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 159 | 51 | | |
| Units: milligrams per deciliter (mg/dL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=159,51) | 1.72 (± 0.51) | 1.77 (± 0.51) | | |
| Change From Baseline at Week 1 (n=158,50) | 0.05 (± 0.22) | 0.03 (± 0.17) | | |
| Change From Baseline at Week 4 (n=157,51) | 0.06 (± 0.21) | 0.11 (± 0.3) | | |
| Change From Baseline at Week 8 (n=147,47) | 0.06 (± 0.21) | 0.09 (± 0.24) | | |
| Change From Baseline at Week 12 (n=137,45) | 0.05 (± 0.24) | 0.08 (± 0.2) | | |
| Change From Baseline at Week 16 (n=134,44) | 0.09 (± 0.3) | 0.09 (± 0.29) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Serum Cystatin C at Weeks 12 and 16

| End point title | Change From Baseline in Serum Cystatin C at Weeks 12 and |
|---|---|

End point description:

Cystatin C is a protein which is mainly used as a biomarker of kidney function. If kidney function and GFR decline, the blood levels of cystatin C rise.

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

End point timeframe:

Baseline, Week 12, and Week 16

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this secondary endpoint. Secondary analyses included tabulations of summary statistics of all continuous secondary endpoints.

| **End point values** | PF-04634817 200 mg/150 mg Daily | Placebo Daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 159 | 51 | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=159,51) | 1.54 (± 0.43) | 1.52 (± 0.41) | | |
| Change From Baseline at Week 12 (n=136,45) | 0.03 (± 0.25) | 0.03 (± 0.21) | | |
| Change From Baseline at Week 16 (n=134,44) | 0.05 (± 0.26) | 0.06 (± 0.25) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Plasma Glycosylated Hemoglobin (HbA1c) at Weeks 4, 8, 12 and 16

| End point title | Change From Baseline in Plasma Glycosylated Hemoglobin (HbA1c) at Weeks 4, 8, 12 and 16[8] |
|---|---|

End point description:

HbA1c is a form of hemoglobin that is measured primarily to identify the average plasma glucose concentration over prolonged periods of time. As the average amount of plasma glucose increases, the fraction of HbA1c increases in a predictable way.

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

End point timeframe:

Baseline, Weeks 4, 8, 12 and 16

Notes:

[8] - 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: No statistical analysis was planned for this secondary endpoint. Secondary analyses included tabulations of summary statistics of all continuous secondary endpoints.

| End point values | PF-04634817 200 mg/150 mg Daily | Placebo Daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 159 | 51 | | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=159,51) | 7.51 (± 1.22) | 7.91 (± 1.42) | | |
| Change From Baseline at Week 4 (n=157,51) | 0.03 (± 0.46) | -0.04 (± 0.46) | | |
| Change From Baseline at Week 8 (n=147,46) | -0.02 (± 0.64) | -0.08 (± 0.71) | | |
| Change From Baseline at Week 12 (n=137,44) | -0.01 (± 0.76) | -0.06 (± 0.81) | | |
| Change From Baseline at Week 16 (n=133,44) | 0.04 (± 0.89) | -0.04 (± 1.13) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Summary of Plasma PF-04634817 Pharmacokinetic (PK) Concentrations at Day 1 and Weeks 1, 4, 8 and 12

| End point title | Summary of Plasma PF-04634817 Pharmacokinetic (PK) Concentrations at Day 1 and Weeks 1, 4, 8 and 12[9] |
|---|---|

End point description:

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

End point timeframe:

1, 2, 4 hours post-dose on Day 1; 2 hours post-dose on Weeks 1, 4, 8 and 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: No statistical analysis was planned for this secondary endpoint. Secondary analyses included tabulations of summary statistics of all continuous secondary endpoints.

| End point values | PF-04634817 150 mg Daily | PF-04634817 200 mg Daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 30 | 140 | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Day 1: 1 Hour Post-Dose (n=29,124) | 434.5 (± 65) | 524.4 (± 83) | | |
| Day 1: 2 Hours Post-Dose (n=30,139) | 579.3 (± 37) | 602.9 (± 52) | | |
| Day 1: 4 Hours Post-Dose (n=29,137) | 497.4 (± 38) | 547.7 (± 46) | | |
| Week 1: Pre-Dose (n=28,131) | 294.4 (± 60) | 231.2 (± 73) | | |
| Week 1: 2 Hours Post-Dose (n=28,132) | 884.8 (± 42) | 865 (± 55) | | |
| Week 4: Pre-Dose (n=25,126) | 231.3 (± 51) | 239.5 (± 87) | | |
| Week 4: 2 Hours Post-Dose (n=24,122) | 785.8 (± 45) | 918 (± 55) | | |
| Week 8: Pre-Dose (n=23,113) | 310.2 (± 79) | 245.2 (± 77) | | |
| Week 8: 2 Hours Post-Dose (n=23,114) | 730 (± 70) | 895 (± 57) | | |
| Week 12 (n=20,113) | 320.1 (± 75) | 252.3 (± 84) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Change From Baseline in Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) at Weeks 1, 4, 8, 12 and 16

| End point title | Change From Baseline in Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) at Weeks 1, 4, 8, 12 and 16[10] |
|---|---|
| End point description: Wk=Week | |
| End point type | Other pre-specified |
| End point timeframe: Baseline, Weeks 1, 4, 8, 12 and 16 | |

Notes:

[10] - 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: No statistical analysis was planned for this safety endpoint. Safety data were summarized using Sponsor Data Standards.

| **End point values** | PF-04634817 200 mg/150 mg Daily | Placebo Daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 170 | 56 | | |
| Units: millimeters of mercury (mm Hg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Supine SBP: Baseline (n=168,53) | 140.4 (± 13.96) | 139.9 (± 13.6) | | |
| Supine SBP:Change From Baseline Wk 1 (n=164,53) | -0.8 (± 12.75) | -1.6 (± 12.87) | | |
| Supine SBP:Change From Baseline Wk 4 (n=154,49) | -0.5 (± 15.43) | -1.6 (± 14.19) | | |
| Supine SBP:Change From Baseline Wk 8 (n=142,47) | -3.4 (± 12.94) | -1.1 (± 13.71) | | |
| Supine SBP:Change From Baseline Wk 12 (n=134,45) | -2 (± 13.28) | -1.3 (± 13.23) | | |
| Supine SBP:Change From Baseline Wk 16 (n=138,45) | -2.4 (± 15.14) | -0.3 (± 14.41) | | |
| Supine DBP: Baseline (n=168,53) | 75.9 (± 8.97) | 77.1 (± 6.88) | | |
| Supine DBP:Change From Baseline Wk 1 (n=164,53) | -0.2 (± 6.94) | -2.7 (± 7.58) | | |
| Supine DBP:Change From Baseline Wk 4 (n=154,49) | 0.1 (± 8.23) | -1.8 (± 7.47) | | |
| Supine DBP:Change From Baseline Wk 8 (n=142,47) | -1.9 (± 7.46) | -1.5 (± 7.05) | | |
| Supine DBP:Change From Baseline Wk 12 (n=134,45) | -0.9 (± 6.88) | -0.2 (± 6.69) | | |
| Supine DBP:Change From Baseline Wk 16 (n=138,45) | -1.7 (± 7.98) | 0.9 (± 8.4) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Change From Baseline in Pulse Rate at Weeks 1, 4, 8, 12 and 16

| End point title | Change From Baseline in Pulse Rate at Weeks 1, 4, 8, 12 and 16[11] |
|---|---|

End point description:

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline, Weeks 1, 4, 8, 12 and 16

Notes:

[11] - 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: No statistical analysis was planned for this safety endpoint. Safety data were summarized using Sponsor Data Standards.

| **End point values** | PF-04634817 200 mg/150 mg Daily | Placebo Daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 170 | 56 | | |
| Units: beats per minute (bpm) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=168,53) | 68.7 (± 9.74) | 69.3 (± 9.3) | | |
| Change From Baseline at Week 1 (n=164,53) | 0.1 (± 5.86) | -0.7 (± 5.63) | | |
| Change From Baseline at Week 4 (n=154,49) | 0.3 (± 6.01) | -1 (± 6.63) | | |
| Change From Baseline at Week 8 (n=142,47) | 0.2 (± 6.54) | 1.4 (± 6.77) | | |
| Change From Baseline at Week 12 (n=134,45) | 0.2 (± 7.03) | 0.5 (± 7.33) | | |
| Change From Baseline at Week 16 (n=138,45) | 1.4 (± 8.22) | -0.1 (± 6.92) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Change From Baseline in Body Weight at Weeks 1, 4, 8, 12 and 16

| End point title | Change From Baseline in Body Weight at Weeks 1, 4, 8, 12 and 16[12] |
|---|---|

End point description:

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline, Weeks 1, 4, 8, 12 and 16

Notes:

[12] - 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: No statistical analysis was planned for this safety endpoint. Safety data were summarized using Sponsor Data Standards.

| **End point values** | PF-04634817 200 mg/150 mg Daily | Placebo Daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 170 | 56 | | |
| Units: kilograms (kg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=167,53) | 93.8 (± 23.97) | 95.1 (± 25.95) | | |
| Change From Baseline at Week 1 (n=163,53) | 0 (± 1.03) | 0.3 (± 1.42) | | |
| Change From Baseline at Week 4 (n=153,49) | 0 (± 1.74) | 0.4 (± 3.29) | | |
| Change From Baseline at Week 8 (n=141,47) | 0.1 (± 2.45) | 0.7 (± 2.74) | | |
| Change From Baseline at Week 12 (n=134,45) | 0.3 (± 2.66) | 0.7 (± 3.02) | | |
| Change From Baseline at Week 16 (n=137,45) | -0.1 (± 2.79) | 0.2 (± 3.37) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Number of Subjects With Laboratory Abnormalities Meeting the Criteria for Potential Clinical Concern

| End point title | Number of Subjects With Laboratory Abnormalities Meeting the Criteria for Potential Clinical Concern[13] |
|---|---|

End point description:

The following laboratory parameters were analyzed for abnormalities at any time point mentioned in the timeframe: clinical chemistry (sodium, potassium, chloride, bicarbonate, phosphate, glucose, blood urea nitrogen [BUN], creatinine, albumin, calcium, bilirubin [total, direct, and indirect], gamma-glutamyl transferase [GGT], alanine aminotransferase [ALT], aspartate aminotransferase [AST], lactic dehydrogenase [LDH], alkaline phosphatase, creatine phosphokinase [CPK], uric acid, amylase and lipase); hematology (hemoglobin, hematocrit, red blood cell [RBC] count, white blood cell [WBC] count with differential, and platelet count); FSH (for postmenopausal women who had been amenorrheic for less than 2 years prior to screening).

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline up to Week 16 (follow-up visit)

Notes:

[13] - 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: No statistical analysis was planned for this safety endpoint. Safety data were summarized

using Sponsor Data Standards.

| End point values | PF-04634817 200 mg/150 mg Daily | Placebo Daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 167 | 53 | | |
| Units: subjects | 154 | 49 | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Number of Subjects With Potentially Clinically Significant Electrocardiogram (ECG) Findings

| End point title | Number of Subjects With Potentially Clinically Significant Electrocardiogram (ECG) Findings[14] |
|---|---|

End point description:

Criteria for potentially clinically important ECG values were defined as: PR interval >=300 milliseconds (msec) or >=25%/50% increase when baseline is >200 msec and ≥50% increase when baseline is less than or equal to (<=)200 msec; QRS interval >=140 msec or >=50% increase from baseline (IFB); QTc >=450 msec or >=30 msec increase; corrected QT interval using Fridericia's formula (QTcF) >=450 msec or >=30 msec increase.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline, Weeks 1, 4 and 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: No statistical analysis was planned for this safety endpoint. Safety data were summarized using Sponsor Data Standards.

| End point values | PF-04634817 200 mg/150 mg Daily | Placebo Daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 170 | 56 | | |
| Units: subjects | | | | |
| Maximum PR Interval >=300 msec (n=164,55) | 3 | 0 | | |
| Maximum QRS Complex >=140 msec (n=169,56) | 2 | 1 | | |
| Maximum QT Interval >=500 msec (n=169,56) | 0 | 0 | | |
| Maximum QTc Interval 450-<480 msec (n=169,56) | 23 | 11 | | |
| Maximum QTc Interval 480-<500 msec (n=169,56) | 4 | 1 | | |
| Maximum QTc Interval >=500 msec (n=169,56) | 0 | 0 | | |
| Maximum QTcF Interval 450-<480 msec (n=169,56) | 11 | 5 | | |

| | | | | |
|---|---|---|---|---|
| Maximum QTcF Interval 480-<500 msec (n=169,56) | 1 | 1 | | |
| Maximum QTcF Interval >=500 msec (n=169,56) | 1 | 0 | | |
| PR Interval >=25/50% IFB (n=163,53) | 3 | 0 | | |
| QRS Complex >=50% IFB (n=169,55) | 3 | 0 | | |
| QTc Interval 30-<60 msec IFB (n=169,55) | 15 | 4 | | |
| QTc Interval >=60 msec IFB (n=169,55) | 0 | 0 | | |
| QTcF Interval 30-<60 msec IFB (n=169,55) | 8 | 3 | | |
| QTcF Interval >=60 msec IFB (n=169,55) | 1 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Number of Subjects With Treatment-Emergent Adverse Events (AEs) or Serious Adverse Events (SAEs)

| End point title | Number of Subjects With Treatment-Emergent Adverse Events (AEs) or Serious Adverse Events (SAEs)[15] |
|---|---|

End point description:

An AE was any untoward medical occurrence without regard to causality in a participant who received study drug. A SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent are 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. AEs included both SAEs and non-serious AEs.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline up to 28 days after last study drug administration

Notes:

[15] - 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: No statistical analysis was planned for this safety endpoint. Safety data were summarized using Sponsor Data Standards.

| **End point values** | PF-04634817 200 mg/150 mg Daily | Placebo Daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 170 | 56 | | |
| Units: subjects | | | | |
| Adverse Events | 106 | 36 | | |
| Serious Adverse Events | 17 | 5 | | |

### Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Number of Subjects With Increased Fasting Blood Glucose

| End point title | Number of Subjects With Increased Fasting Blood Glucose[16] |
|---|---|

End point description:

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Baseline up to Week 16 (follow-up visit)

Notes:

[16] - 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: No statistical analysis was planned for this safety endpoint. Safety data were summarized using Sponsor Data Standards.

| **End point values** | PF-04634817 200 mg/150 mg Daily | Placebo Daily | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 167 | 53 | | |
| Units: subjects | 1 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to 28 days after last study drug administration

Adverse event reporting additional description:

The same event may appear as both an AE and a 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 | 17.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | PF-04634817 150 mg |

Reporting group description:

Subjects with estimated glomerular filtration rate (eGFR) values of 20 to less than (<)30 milliliters/minute (mL/min)/1.73 square meter (m^2) were dosed orally at 150 mg once daily for 12 weeks.

| | |
|---|---|
| Reporting group title | Placebo |

Reporting group description:

Subjects were dosed orally with matching placebo tablets once daily for 12 weeks.

| | |
|---|---|
| Reporting group title | PF-04634817 200 mg |

Reporting group description:

Subjects with eGFR values of 30 to 75 mL/min/1.73 m^2 were dosed orally at 200 mg once daily for 12 weeks.

| Serious adverse events | PF-04634817 150 mg | Placebo | PF-04634817 200 mg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 30 (20.00%) | 5 / 56 (8.93%) | 11 / 140 (7.86%) |
| number of deaths (all causes) | 0 | 1 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 56 (0.00%) | 1 / 140 (0.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 56 (0.00%) | 2 / 140 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 56 (0.00%) | 1 / 140 (0.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 56 (0.00%) | 1 / 140 (0.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Social circumstances | | | |
| Homicide | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 56 (1.79%) | 0 / 140 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 56 (1.79%) | 0 / 140 (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 |
| Cardiac disorders | | | |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 56 (0.00%) | 0 / 140 (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 |
| Nervous system disorders | | | |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 56 (0.00%) | 1 / 140 (0.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 56 (0.00%) | 0 / 140 (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 |
| Gastrointestinal disorders | | | |
| Gastritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 56 (0.00%) | 1 / 140 (0.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 56 (0.00%) | 1 / 140 (0.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 56 (0.00%) | 1 / 140 (0.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 56 (0.00%) | 0 / 140 (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 |
| Erythrodermic psoriasis | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 56 (0.00%) | 0 / 140 (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 |
| Renal and urinary disorders | | | |
| Renal failure acute | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 56 (0.00%) | 2 / 140 (1.43%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Gouty arthritis | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 56 (0.00%) | 0 / 140 (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 | | | |
| Cellulitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 56 (1.79%) | 0 / 140 (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 |
| Localised infection | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 56 (1.79%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 1 / 56 (1.79%) | 1 / 140 (0.71%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic shock | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 56 (0.00%) | 0 / 140 (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 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 56 (0.00%) | 1 / 140 (0.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 56 (0.00%) | 0 / 140 (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 |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 56 (0.00%) | 0 / 140 (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 |

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

| **Non-serious adverse events** | PF-04634817 150 mg | Placebo | PF-04634817 200 mg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 11 / 30 (36.67%) | 15 / 56 (26.79%) | 40 / 140 (28.57%) |
| Investigations | | | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 56 (0.00%) | 1 / 140 (0.71%) |
| occurrences (all) | 2 | 0 | 1 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 3 / 56 (5.36%) | 6 / 140 (4.29%) |
| occurrences (all) | 2 | 3 | 6 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 1 / 56 (1.79%) | 4 / 140 (2.86%) |
| occurrences (all) | 2 | 1 | 7 |
| General disorders and administration site conditions | | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | 4 / 56 (7.14%) | 8 / 140 (5.71%) |
| occurrences (all) | 3 | 4 | 9 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 3 / 56 (5.36%) | 12 / 140 (8.57%) |
| occurrences (all) | 2 | 3 | 12 |
| Nausea | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 2 / 56 (3.57%) | 5 / 140 (3.57%) |
| occurrences (all) | 2 | 2 | 7 |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 1 / 56 (1.79%) | 0 / 140 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 1 / 56 (1.79%) | 2 / 140 (1.43%) |
| occurrences (all) | 2 | 1 | 2 |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 3 / 56 (5.36%) | 6 / 140 (4.29%) |
| occurrences (all) | 2 | 3 | 8 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 2 / 56 (3.57%) | 5 / 140 (3.57%) |
| occurrences (all) | 2 | 2 | 6 |
| Metabolism and nutrition disorders | | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 1 / 56 (1.79%) | 1 / 140 (0.71%) |
| occurrences (all) | 2 | 1 | 1 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 1 / 56 (1.79%) | 2 / 140 (1.43%) |
| occurrences (all) | 3 | 1 | 3 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 30 October 2012 | Electrocardiogram (ECG) assessments were modified and guidance on participant withdrawal ("stopping rules") was included as requested by the Food and Drug Administration (FDA). Exclusion criterion was loosened to exclude subjects with a history of proteinuria >8.5 g/day. |
| 27 September 2013 | Dose adjustment to 150 mg once daily (QD) in subjects with eGFR <30 mL/min.1.73 m^2 was added. Screening window was extended to 35 days to accomodate additional TB testing and chest X-ray if necessary. Inclusion criterion for eGFR was changed from 30-59 mL/min/1.73 m^2 to 20-75 mL/min/1.73 m^2 based on the results from a previous study. Inclusion criterion of UPCR >=390 mg/g was removed. Lifestyle guidelines relating to condom use by male subjects was removed. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported