



Clinical trial results:

A Multicenter, Open-Label, Multiple Ascending Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Efficacy of Subcutaneous or Intravenous PF-06741086 in Subjects With Severe Hemophilia

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2016-001885-27 |
| Trial protocol | PL ES FR BG HR |
| Global end of trial date | 03 December 2018 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 02 December 2019 |
| First version publication date | 02 December 2019 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | B7841002 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02974855 |
| 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 | 23 May 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 03 December 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 03 December 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to determine the safety and tolerability of multiple doses of PF-06741086 administered to severe hemophilia A and B subjects with and without inhibitors to Factor VIII (FVIII) or Factor IX (FIX).

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 Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of subjects.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 08 March 2017 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy, Safety |
| Long term follow-up duration | 1 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | Chile: 10 |
| Country: Number of subjects enrolled | Croatia: 2 |
| Country: Number of subjects enrolled | Poland: 1 |
| Country: Number of subjects enrolled | South Africa: 10 |
| Country: Number of subjects enrolled | Switzerland: 1 |
| Country: Number of subjects enrolled | United States: 2 |
| Worldwide total number of subjects | 26 |
| EEA total number of subjects | 3 |

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) | 26 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 27 subjects were enrolled in the study and assigned to 1 of 4 cohorts. Only 26 subjects received the study treatment and 1 subject withdrew after randomization but prior to dosing.

Period 1

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

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | PF-06741086 300 mg SC QW Non-Inhibitor |

Arm description:

Subjects without inhibitors to Factor VIII (FVIII) or Factor IX (FIX) in this cohort received PF-06741086 300 mg subcutaneously (SC) once weekly (QW) from Day 1 to Day 78.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | PF-06741086 Solution for Injection, 100 mg/mL |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

PF-06741086 300 mg was administered subcutaneously every week.

| | |
|------------------|--|
| Arm title | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor |
|------------------|--|

Arm description:

Subjects without inhibitors to FVIII or FIX in this cohort received PF-06741086 300 mg loading dose on Day 1 and 150 mg SC QW from Day 8 to Day 78.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | PF-06741086 Solution for Injection, 100 mg/mL |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

PF-06741086 300 mg loading dose, PF-06741086 150 mg was administered subcutaneously every week.

| | |
|------------------|--|
| Arm title | PF-06741086 450 mg SC QW Non-Inhibitor |
|------------------|--|

Arm description:

Subjects without inhibitors to FVIII or FIX in this cohort received PF-06741086 450 mg SC QW from Day 1 to Day 78.

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

| | |
|--|---|
| Investigational medicinal product name | PF-06741086 Solution for Injection, 100 mg/mL |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: PF-06741086 450 mg was administered subcutaneously every week. | |
| Arm title | PF-06741086 300 mg SC QW Inhibitor |

Arm description:

Subjects with inhibitors to FVIII or FIX in this cohort received PF-06741086 300 mg SC QW from Day 1 to Day 78.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | PF-06741086 Solution for Injection, 100 mg/mL |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

PF-06741086 300 mg was administered subcutaneously every week.

| Number of subjects in period 1 | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor |
|---------------------------------------|--|--|--|
| Started | 7 | 6 | 6 |
| Completed | 7 | 5 | 6 |
| Not completed | 0 | 1 | 0 |
| Adverse event, non-fatal | - | 1 | - |

| Number of subjects in period 1 | PF-06741086 300 mg SC QW Inhibitor |
|---------------------------------------|------------------------------------|
| Started | 7 |
| Completed | 6 |
| Not completed | 1 |
| Adverse event, non-fatal | 1 |

Baseline characteristics

Reporting groups

| | |
|---|--|
| Reporting group title | PF-06741086 300 mg SC QW Non-Inhibitor |
| Reporting group description: Subjects without inhibitors to Factor VIII (FVIII) or Factor IX (FIX) in this cohort received PF-06741086 300 mg subcutaneously (SC) once weekly (QW) from Day 1 to Day 78. | |
| Reporting group title | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor |
| Reporting group description: Subjects without inhibitors to FVIII or FIX in this cohort received PF-06741086 300 mg loading dose on Day 1 and 150 mg SC QW from Day 8 to Day 78. | |
| Reporting group title | PF-06741086 450 mg SC QW Non-Inhibitor |
| Reporting group description: Subjects without inhibitors to FVIII or FIX in this cohort received PF-06741086 450 mg SC QW from Day 1 to Day 78. | |
| Reporting group title | PF-06741086 300 mg SC QW Inhibitor |
| Reporting group description: Subjects with inhibitors to FVIII or FIX in this cohort received PF-06741086 300 mg SC QW from Day 1 to Day 78. | |

| Reporting group values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor |
|--------------------------------------|--|--|--|
| Number of subjects | 7 | 6 | 6 |
| Age Categorical Units: Subjects | | | |
| <=18 years | 0 | 0 | 0 |
| Between 18 and 65 years | 7 | 6 | 6 |
| >=65 years | 0 | 0 | 0 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 31.9 | 28.7 | 41.7 |
| standard deviation | ± 8.17 | ± 8.31 | ± 15.87 |
| Sex: Female, Male Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 7 | 6 | 6 |
| Race (NIH/OMB) Units: Subjects | | | |
| White | 3 | 2 | 6 |
| Black or African American | 4 | 4 | 0 |
| Other | 0 | 0 | 0 |

| Reporting group values | PF-06741086 300 mg SC QW Inhibitor | Total | |
|------------------------------------|------------------------------------|-------|--|
| Number of subjects | 7 | 26 | |
| Age Categorical Units: Subjects | | | |
| <=18 years | 0 | 0 | |
| Between 18 and 65 years | 7 | 26 | |

| | | | |
|------------|---|---|--|
| >=65 years | 0 | 0 | |
|------------|---|---|--|

| | | | |
|---|----------------|----|--|
| Age Continuous Units: Years arithmetic mean standard deviation | 44.1 ± 9.44 | - | |
| Sex: Female, Male Units: Subjects | | | |
| Female | 0 | 0 | |
| Male | 7 | 26 | |
| Race (NIH/OMB) Units: Subjects | | | |
| White | 3 | 14 | |
| Black or African American | 4 | 12 | |
| Other | 0 | 0 | |

Subject analysis sets

| | |
|---|-------------------------------|
| Subject analysis set title | Overall PF-06741086 300 mg SC |
| Subject analysis set type | Full analysis |
| Subject analysis set description: The overall PF-06741086 300 mg SC group combined subjects from both the PF-06741086 300 mg SC QW non-inhibitor and inhibitor dose cohorts. | |
| Subject analysis set title | Total |
| Subject analysis set type | Full analysis |
| Subject analysis set description: The total group combined subjects from all PF-06741086 cohorts in this study. | |

| Reporting group values | Overall PF-06741086 300 mg SC | Total | |
|---|-------------------------------|-----------------|--|
| Number of subjects | 14 | 26 | |
| Age Categorical Units: Subjects | | | |
| <=18 years | 0 | 0 | |
| Between 18 and 65 years | 14 | 26 | |
| >=65 years | 0 | 0 | |
| Age Continuous Units: Years arithmetic mean standard deviation | 38.0 ± 10.61 | 36.7 ± 12.05 | |
| Sex: Female, Male Units: Subjects | | | |
| Female | 0 | 0 | |
| Male | 14 | 26 | |
| Race (NIH/OMB) Units: Subjects | | | |
| White | 6 | 14 | |
| Black or African American | 8 | 12 | |
| Other | 0 | 0 | |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | PF-06741086 300 mg SC QW Non-Inhibitor |
| Reporting group description: Subjects without inhibitors to Factor VIII (FVIII) or Factor IX (FIX) in this cohort received PF-06741086 300 mg subcutaneously (SC) once weekly (QW) from Day 1 to Day 78. | |
| Reporting group title | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor |
| Reporting group description: Subjects without inhibitors to FVIII or FIX in this cohort received PF-06741086 300 mg loading dose on Day 1 and 150 mg SC QW from Day 8 to Day 78. | |
| Reporting group title | PF-06741086 450 mg SC QW Non-Inhibitor |
| Reporting group description: Subjects without inhibitors to FVIII or FIX in this cohort received PF-06741086 450 mg SC QW from Day 1 to Day 78. | |
| Reporting group title | PF-06741086 300 mg SC QW Inhibitor |
| Reporting group description: Subjects with inhibitors to FVIII or FIX in this cohort received PF-06741086 300 mg SC QW from Day 1 to Day 78. | |
| Subject analysis set title | Overall PF-06741086 300 mg SC |
| Subject analysis set type | Full analysis |
| Subject analysis set description: The overall PF-06741086 300 mg SC group combined subjects from both the PF-06741086 300 mg SC QW non-inhibitor and inhibitor dose cohorts. | |
| Subject analysis set title | Total |
| Subject analysis set type | Full analysis |
| Subject analysis set description: The total group combined subjects from all PF-06741086 cohorts in this study. | |

Primary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

| | |
|---|--|
| End point title | Number of Subjects With Treatment Emergent Adverse Events (TEAEs) ^[1] |
| End point description: An adverse event (AE) was any untoward medical occurrence in a clinical investigation participant administered a product; the event did not need to have a causal relationship with the treatment. A serious adverse event (SAE) was any untoward medical occurrence at any dose that resulted in death; was life threatening; required inpatient hospitalization or prolongation of existing hospitalization; resulted in persistent or significant disability/incapacity; resulted in congenital anomaly/birth defect. AEs included both SAEs and AEs. TEAEs were AEs occurred following the start of treatment or AEs increasing in severity during treatment. Severe TEAEs were TEAEs that interfered significantly with participants' usual function. Treatment-related TEAEs were determined by the investigator. | |
| End point type | Primary |
| End point timeframe: Study Day 1 to Day 113 Visit | |

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 planned for this endpoint

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|-------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 6 | 7 |
| Units: Subjects | | | | |
| All-causalities TEAE | 7 | 4 | 6 | 4 |
| Treatment-related TEAE | 4 | 4 | 3 | 3 |
| All-causalities serious TEAE | 1 | 1 | 1 | 1 |
| Treatment-related serious TEAE | 0 | 0 | 0 | 0 |
| All-causalities Grade 3 or 4 TEAE | 0 | 0 | 2 | 2 |
| Treatment-related Grade 3 or 4 TEAE | 0 | 0 | 2 | 2 |

| End point values | Overall PF- 06741086 300 mg SC | Total | | |
|-------------------------------------|--------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 14 | 26 | | |
| Units: Subjects | | | | |
| All-causalities TEAE | 11 | 21 | | |
| Treatment-related TEAE | 7 | 14 | | |
| All-causalities serious TEAE | 2 | 4 | | |
| Treatment-related serious TEAE | 0 | 0 | | |
| All-causalities Grade 3 or 4 TEAE | 2 | 4 | | |
| Treatment-related Grade 3 or 4 TEAE | 2 | 4 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Discontinued From Study due to TEAEs

| | |
|-----------------|--|
| End point title | Number of Subjects Discontinued From Study due to TEAEs ^[2] |
|-----------------|--|

End point description:

An AE was any untoward medical occurrence in a clinical investigation participant administered a product; the event did not need to have a causal relationship with the treatment. TEAEs were AEs occurred following the start of treatment or AEs increasing in severity during treatment. Treatment-related TEAEs were determined by the investigator.

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

End point timeframe:

Study Day 1 to Day 113 Visit

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 planned for this endpoint

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|-----------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 6 | 7 |
| Units: Subjects | | | | |
| All-causalities TEAE | 0 | 1 | 0 | 1 |
| Treatment-related TEAE | 0 | 1 | 0 | 1 |

| End point values | Overall PF- 06741086 300 mg SC | Total | | |
|-----------------------------|--------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 14 | 26 | | |
| Units: Subjects | | | | |
| All-causalities TEAE | 1 | 2 | | |
| Treatment-related TEAE | 1 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Abnormal Laboratory Findings-Hematology

| | |
|-----------------|--|
| End point title | Number of Subjects With Abnormal Laboratory Findings-Hematology ^[3] |
|-----------------|--|

End point description:

Hematology evaluation included: hemoglobin, hematocrit, erythrocytes, platelets, leukocytes, lymphocytes, neutrophils, basophils, eosinophils and monocytes. Pre-defined criteria for hemoglobin and hematocrit: $<0.8 \times \text{lower limit of normal (LLN)}$ or $<0.8 \times \text{Baseline}$ ($\text{Baseline} < 1.0 \times \text{LLN}$); for platelets: $<100,000 \times 10^3/\text{mm}^3$ or $\leq 0.77 \times \text{Baseline}$ ($\text{Baseline} < 1.0 \times \text{LLN}$).

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

End point timeframe:

Baseline to Study Day 113 Visit

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 planned for this endpoint

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 6 | 7 |
| Units: Subjects | | | | |
| Hemoglobin meeting pre-defined criteria | 0 | 0 | 0 | 0 |
| Hematocrit meeting pre-defined criteria | 0 | 0 | 0 | 0 |
| Erythrocytes $<0.8 \times \text{LLN}$ | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| Platelets meeting pre-defined criteria | 0 | 0 | 0 | 0 |
| Leukocytes <0.6*LLN | 0 | 0 | 0 | 0 |
| Leukocytes >1.5*upper limit of normal (ULN) | 0 | 0 | 0 | 0 |
| Lymphocytes <0.8*LLN | 0 | 1 | 0 | 0 |
| Lymphocytes >1.2*ULN | 0 | 0 | 0 | 0 |
| Neutrophils <0.8*LLN | 1 | 2 | 0 | 0 |
| Neutrophils >1.2*ULN | 0 | 0 | 0 | 0 |
| Basophils >1.2*ULN | 0 | 0 | 0 | 0 |
| Eosinophils >1.2*ULN | 0 | 0 | 0 | 0 |
| Monocytes >1.2*ULN | 0 | 0 | 0 | 0 |

| End point values | Overall PF-06741086 300 mg SC | Total | | |
|---|-------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 14 | 26 | | |
| Units: Subjects | | | | |
| Hemoglobin meeting pre-defined criteria | 0 | 0 | | |
| Hematocrit meeting pre-defined criteria | 0 | 0 | | |
| Erythrocytes <0.8*LLN | 0 | 0 | | |
| Platelets meeting pre-defined criteria | 0 | 0 | | |
| Leukocytes <0.6*LLN | 0 | 0 | | |
| Leukocytes >1.5*upper limit of normal (ULN) | 0 | 0 | | |
| Lymphocytes <0.8*LLN | 0 | 1 | | |
| Lymphocytes >1.2*ULN | 0 | 0 | | |
| Neutrophils <0.8*LLN | 1 | 3 | | |
| Neutrophils >1.2*ULN | 0 | 0 | | |
| Basophils >1.2*ULN | 0 | 0 | | |
| Eosinophils >1.2*ULN | 0 | 0 | | |
| Monocytes >1.2*ULN | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Abnormal Laboratory Findings-Clinical Chemistry

| | |
|-----------------|--|
| End point title | Number of Subjects With Abnormal Laboratory Findings-Clinical Chemistry ^[4] |
|-----------------|--|

End point description:

Clinical chemistry evaluation included bilirubin, direct and indirect bilirubin, aspartate aminotransferase, alanine aminotransferase, gamma glutamyl transferase, alkaline phosphatase, protein, albumin, urea nitrogen, creatinine, urate, triglycerides, sodium, potassium, chloride, calcium, bicarbonate, glucose, creatine kinase, troponin I, cholesterol and fibrinogen.

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

End point timeframe:

Baseline to Study Day 113

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 planned for this endpoint

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|-------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[5] | 6 ^[6] | 6 ^[7] | 7 ^[8] |
| Units: Subjects | | | | |
| Bilirubin >1.5*ULN | 0 | 0 | 0 | 0 |
| Direct Bilirubin >1.5*ULN | 0 | 0 | 0 | 0 |
| Indirect Bilirubin >1.5*ULN | 0 | 0 | 0 | 0 |
| Aspartate Aminotransferase >3.0*ULN | 0 | 0 | 1 | 0 |
| Alanine Aminotransferase >3.0* ULN | 1 | 1 | 1 | 0 |
| Gamma Glutamyl Transferase >3.0*ULN | 0 | 1 | 0 | 0 |
| Alkaline Phosphatase | 0 | 0 | 0 | 0 |
| Protein <0.8*LLN | 0 | 0 | 0 | 0 |
| Protein >1.2*ULN | 0 | 0 | 0 | 0 |
| Albumin <0.8*LLN | 0 | 0 | 0 | 0 |
| Albumin >1.2*ULN | 0 | 0 | 0 | 0 |
| Urea Nitrogen >1.3*ULN | 0 | 0 | 0 | 0 |
| Creatinine >1.3*ULN | 0 | 0 | 0 | 0 |
| Urate >1.2*ULN | 0 | 0 | 0 | 2 |
| Triglycerides >1.3*ULN | 0 | 0 | 0 | 0 |
| Sodium <0.95*LLN | 0 | 0 | 0 | 0 |
| Sodium >1.05*ULN | 0 | 0 | 0 | 0 |
| Potassium <0.9*LLN | 1 | 0 | 0 | 0 |
| Potassium >1.1*ULN | 0 | 0 | 0 | 0 |
| Chloride <0.9*LLN | 0 | 0 | 0 | 0 |
| Chloride >1.1*ULN | 0 | 0 | 0 | 0 |
| Calcium <0.9*LLN | 0 | 0 | 0 | 0 |
| Calcium >1.1*ULN | 0 | 0 | 0 | 0 |
| Bicarbonate <0.9*LLN | 2 | 1 | 0 | 0 |
| Bicarbonate >1.1*ULN | 0 | 0 | 0 | 0 |
| Glucose <0.6*LLN | 0 | 0 | 0 | 0 |
| Glucose >1.5*ULN | 0 | 0 | 2 | 1 |
| Creatine Kinase >2.0*ULN | 0 | 0 | 0 | 0 |
| Troponin I >1.0*ULN | 1 | 1 | 0 | 2 |
| Cholesterol >1.3*ULN | 0 | 0 | 0 | 0 |
| Fibrinogen <=0.5*LLN | 0 | 0 | 0 | 1 |

Notes:

[5] - Not all subjects had data for some specific categories.

[6] - Not all subjects had data for some specific categories.

[7] - Not all subjects had data for some specific categories.

[8] - Not all subjects had data for some specific categories.

| End point values | Overall PF- 06741086 300 mg SC | Total | | |
|------------------|--------------------------------------|-------|--|--|
|------------------|--------------------------------------|-------|--|--|

| Subject group type | Subject analysis set | Subject analysis set | | |
|-------------------------------------|----------------------|----------------------|--|--|
| Number of subjects analysed | 14 ^[9] | 26 ^[10] | | |
| Units: Subjects | | | | |
| Bilirubin >1.5*ULN | 0 | 0 | | |
| Direct Bilirubin >1.5*ULN | 0 | 0 | | |
| Indirect Bilirubin >1.5*ULN | 0 | 0 | | |
| Aspartate Aminotransferase >3.0*ULN | 0 | 1 | | |
| Alanine Aminotransferase >3.0* ULN | 1 | 3 | | |
| Gamma Glutamyl Transferase >3.0*ULN | 0 | 1 | | |
| Alkaline Phosphatase | 0 | 0 | | |
| Protein <0.8*LLN | 0 | 0 | | |
| Protein >1.2*ULN | 0 | 0 | | |
| Albumin <0.8*LLN | 0 | 0 | | |
| Albumin >1.2*ULN | 0 | 0 | | |
| Urea Nitrogen >1.3*ULN | 0 | 0 | | |
| Creatinine >1.3*ULN | 0 | 0 | | |
| Urate >1.2*ULN | 2 | 2 | | |
| Triglycerides >1.3*ULN | 0 | 0 | | |
| Sodium <0.95*LLN | 0 | 0 | | |
| Sodium >1.05*ULN | 0 | 0 | | |
| Potassium <0.9*LLN | 1 | 1 | | |
| Potassium >1.1*ULN | 0 | 0 | | |
| Chloride <0.9*LLN | 0 | 0 | | |
| Chloride >1.1*ULN | 0 | 0 | | |
| Calcium <0.9*LLN | 0 | 0 | | |
| Calcium >1.1*ULN | 0 | 0 | | |
| Bicarbonate <0.9*LLN | 2 | 3 | | |
| Bicarbonate >1.1*ULN | 0 | 0 | | |
| Glucose <0.6*LLN | 0 | 0 | | |
| Glucose >1.5*ULN | 1 | 3 | | |
| Creatine Kinase >2.0*ULN | 0 | 0 | | |
| Troponin I >1.0*ULN | 3 | 4 | | |
| Cholesterol >1.3*ULN | 0 | 0 | | |
| Fibrinogen <=0.5*LLN | 1 | 1 | | |

Notes:

[9] - Not all subjects had data for some specific categories.

[10] - Not all subjects had data for some specific categories.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Abnormal Laboratory Findings-Urinalysis

| | |
|--|---|
| End point title | Number of Subjects With Abnormal Laboratory Findings-Urinalysis ^[11] |
| End point description: | |
| Urinalysis included: pH, urine glucose, ketones, urine protein, urine hemoglobin, urobilinogen, urine bilirubin, nitrite, leukocyte esterase, urine erythrocytes, urine leukocytes and bacteria. | |
| End point type | Primary |
| End point timeframe: | |
| Baseline to Study Day 113 Visit | |

Notes:

[11] - 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 planned for this endpoint

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|---------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[12] | 6 ^[13] | 6 ^[14] | 7 ^[15] |
| Units: Subjects | | | | |
| pH (Scalar) <4.5 | 0 | 0 | 0 | 0 |
| pH (Scalar) >8 | 0 | 0 | 0 | 0 |
| Urine glucose >=1 | 0 | 0 | 1 | 0 |
| Ketones (Scalar) >=1 | 0 | 0 | 1 | 1 |
| Urine protein >=1 | 0 | 0 | 0 | 1 |
| Urine hemoglobin (Scalar) >=1 | 0 | 0 | 0 | 0 |
| Urobilinogen >=1 | 0 | 0 | 0 | 0 |
| Urine bilirubin (Scalar) >=1 | 0 | 0 | 0 | 0 |
| Nitrite (Scalar) >=1 | 0 | 0 | 0 | 0 |
| Leukocyte esterase (Scalar) >=1 | 1 | 1 | 0 | 1 |
| Urine erythrocytes (/HPF) >=20 | 0 | 0 | 0 | 0 |
| Urine leukocytes (/HPF) >=20 | 0 | 1 | 0 | 1 |
| Bacteria (/HPF) >20 | 0 | 0 | 0 | 0 |

Notes:

[12] - Not all subjects had data for some specific categories.

[13] - Not all subjects had data for some specific categories.

[14] - Not all subjects had data for some specific categories.

[15] - Not all subjects had data for some specific categories.

| End point values | Overall PF- 06741086 300 mg SC | Total | | |
|---------------------------------|--------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 14 ^[16] | 26 ^[17] | | |
| Units: Subjects | | | | |
| pH (Scalar) <4.5 | 0 | 0 | | |
| pH (Scalar) >8 | 0 | 0 | | |
| Urine glucose >=1 | 0 | 1 | | |
| Ketones (Scalar) >=1 | 1 | 2 | | |
| Urine protein >=1 | 1 | 1 | | |
| Urine hemoglobin (Scalar) >=1 | 0 | 0 | | |
| Urobilinogen >=1 | 0 | 0 | | |
| Urine bilirubin (Scalar) >=1 | 0 | 0 | | |
| Nitrite (Scalar) >=1 | 0 | 0 | | |
| Leukocyte esterase (Scalar) >=1 | 2 | 3 | | |
| Urine erythrocytes (/HPF) >=20 | 0 | 0 | | |
| Urine leukocytes (/HPF) >=20 | 1 | 2 | | |
| Bacteria (/HPF) >20 | 0 | 0 | | |

Notes:

[16] - Not all subjects had data for some specific categories.

[17] - Not all subjects had data for some specific categories.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline for Globulin by Dose Cohort

| | |
|-----------------|--|
| End point title | Change From Baseline for Globulin by Dose Cohort ^[18] |
|-----------------|--|

End point description:

Blood samples were obtained to determine globulin level in serum, total globulin was derived as total protein other than albumin.

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

End point timeframe:

Baseline, Study Day 8, 15, 22, 29, 57, 85 and 113.

Notes:

[18] - 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 planned for this endpoint

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[19] | 6 ^[20] | 6 ^[21] | 7 ^[22] |
| Units: gram/liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Globulin, Change at Day 8 | -0.3 (± 3.04) | -1.7 (± 3.93) | -1.3 (± 2.73) | 0.4 (± 2.51) |
| Globulin, Change at Day 15 | -0.7 (± 2.06) | -0.8 (± 2.32) | -1.3 (± 2.50) | -1.3 (± 3.35) |
| Globulin, Change at Day 22 | -1.6 (± 2.82) | -0.5 (± 1.52) | -1.5 (± 3.08) | -0.6 (± 4.12) |
| Globulin, Change at Day 29 | -0.3 (± 3.27) | -0.3 (± 3.08) | 0.2 (± 1.10) | -1.3 (± 2.75) |
| Globulin, Change at Day 57 | 0.7 (± 3.72) | 1.8 (± 2.99) | -0.3 (± 1.63) | -0.7 (± 2.94) |
| Globulin, Change at Day 85 | 1.3 (± 3.15) | -1.4 (± 4.77) | -0.5 (± 3.02) | 1.0 (± 2.61) |
| Globulin, Change at Day 113 | -0.3 (± 3.15) | -1.2 (± 4.67) | 0.5 (± 2.65) | -0.8 (± 3.06) |

Notes:

[19] - Not all subjects had data for some specific rows of time points.

[20] - Not all subjects had data for some specific rows of time points.

[21] - Not all subjects had data for some specific rows of time points.

[22] - Not all subjects had data for some specific rows of time points.

| End point values | Overall PF- 06741086 300 mg SC | Total | | |
|--------------------------------------|--------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 14 ^[23] | 26 ^[24] | | |
| Units: gram/liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Globulin, Change at Day 8 | 0.1 (± 2.70) | -0.7 (± 3.01) | | |
| Globulin, Change at Day 15 | -1.0 (± 2.69) | -1.0 (± 2.47) | | |

| | | | | |
|-----------------------------|---------------|---------------|--|--|
| Globulin, Change at Day 22 | -1.1 (± 3.43) | -1.0 (± 2.93) | | |
| Globulin, Change at Day 29 | -0.8 (± 2.91) | -0.5 (± 2.62) | | |
| Globulin, Change at Day 57 | 0.0 (± 3.28) | 0.4 (± 2.90) | | |
| Globulin, Change at Day 85 | 1.2 (± 2.79) | 0.2 (± 3.35) | | |
| Globulin, Change at Day 113 | -0.5 (± 2.99) | -0.5 (± 3.33) | | |

Notes:

[23] - Not all subjects had data for some specific rows of time points.

[24] - Not all subjects had data for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline for Prothrombin International Normalized Ratio (PT/INR) by Dose Cohort

| | |
|-----------------|---|
| End point title | Change From Baseline for Prothrombin International Normalized Ratio (PT/INR) by Dose Cohort ^[25] |
|-----------------|---|

End point description:

Blood samples were obtained to evaluate this ratio. The prothrombin time (PT) is a test that helps evaluate your ability to appropriately form blood clots. The international normalized ratio (INR) is a calculation based on results of a PT that is used to monitor individuals who are being treated with the blood-thinning medication (anticoagulant) warfarin (Coumadin®).

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

End point timeframe:

Baseline, Study Day 8, 15, 22, 29, 57, 85 and 113.

Notes:

[25] - 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 planned for this endpoint

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[26] | 6 ^[27] | 6 ^[28] | 7 ^[29] |
| Units: Ratio | | | | |
| arithmetic mean (standard deviation) | | | | |
| PT/INR, Change at Day 8 | -0.03 (± 0.049) | -0.02 (± 0.041) | 0.05 (± 0.138) | 0.03 (± 0.138) |
| PT/INR, Change at Day 15 | 0.03 (± 0.076) | 0.00 (± 0.063) | 0.02 (± 0.041) | 0.00 (± 0.082) |
| PT/INR, Change at Day 22 | 0.03 (± 0.095) | 0.00 (± 0.063) | -0.02 (± 0.041) | -0.01 (± 0.069) |
| PT/INR, Change at Day 29 | 0.03 (± 0.082) | -0.02 (± 0.041) | 0.00 (± 0.063) | 0.00 (± 0.115) |
| PT/INR, Change at Day 57 | 0.00 (± 0.126) | -0.03 (± 0.052) | 0.00 (± 0.063) | -0.02 (± 0.075) |
| PT/INR, Change at Day 85 | -0.01 (± 0.107) | 0.04 (± 0.152) | -0.02 (± 0.075) | -0.03 (± 0.082) |
| PT/INR, Change at Day 113 | 0.06 (± 0.127) | -0.03 (± 0.052) | -0.05 (± 0.058) | 0.07 (± 0.052) |

Notes:

[26] - Not all subjects had data for some specific rows of time points.

[27] - Not all subjects had data for some specific rows of time points.

[28] - Not all subjects had data for some specific rows of time points.

[29] - Not all subjects had data for some specific rows of time points.

| End point values | Overall PF-06741086 300 mg SC | Total | | |
|--------------------------------------|-------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 14 ^[30] | 26 ^[31] | | |
| Units: Ratio | | | | |
| arithmetic mean (standard deviation) | | | | |
| PT/INR, Change at Day 8 | 0.00 (± 0.104) | 0.01 (± 0.102) | | |
| PT/INR, Change at Day 15 | 0.01 (± 0.077) | 0.01 (± 0.065) | | |
| PT/INR, Change at Day 22 | 0.01 (± 0.083) | 0.00 (± 0.069) | | |
| PT/INR, Change at Day 29 | 0.02 (± 0.099) | 0.00 (± 0.079) | | |
| PT/INR, Change at Day 57 | -0.01 (± 0.100) | -0.01 (± 0.080) | | |
| PT/INR, Change at Day 85 | -0.02 (± 0.093) | -0.01 (± 0.102) | | |
| PT/INR, Change at Day 113 | 0.06 (± 0.096) | 0.02 (± 0.094) | | |

Notes:

[30] - Not all subjects had data for some specific rows of time points.

[31] - Not all subjects had data for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline for Activated Partial Thromboplastin Time (aPTT) by Dose Cohort

| | |
|-----------------|--|
| End point title | Change From Baseline for Activated Partial Thromboplastin Time (aPTT) by Dose Cohort ^[32] |
|-----------------|--|

End point description:

The activated partial thromboplastin time (aPTT) is a screening test that helps evaluate a person's ability to appropriately form blood clots. It measures the number of seconds it takes for a clot to form in a sample of blood after substances (reagents) are added. Blood sample were obtained to evaluate aPTT.

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

End point timeframe:

Baseline, Study Day 8, 15, 22, 29, 57, 85 and 113.

Notes:

[32] - 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 planned for this endpoint

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|--------------------------------------|--|--|--|------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[33] | 6 ^[34] | 6 ^[35] | 7 ^[36] |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| aPTT, Change at Day 8 | 8.49 (± 17.017) | 10.63 (± 11.634) | 11.03 (± 15.467) | -12.26 (± 7.082) |
| aPTT, Change at Day 15 | 9.50 (± 10.907) | 12.50 (± 15.303) | 1.20 (± 20.075) | -10.26 (± 6.757) |

| | | | | |
|-------------------------|------------------|------------------|------------------|-------------------|
| aPTT, Change at Day 22 | 14.79 (± 10.799) | 12.15 (± 15.232) | 4.50 (± 9.765) | -11.77 (± 11.247) |
| aPTT, Change at Day 29 | 13.42 (± 11.102) | 9.85 (± 15.999) | 10.13 (± 10.250) | -12.87 (± 11.390) |
| aPTT, Change at Day 57 | 13.65 (± 13.378) | 14.25 (± 14.061) | 7.82 (± 11.580) | -9.13 (± 8.390) |
| aPTT, Change at Day 85 | 9.00 (± 10.928) | 3.84 (± 18.089) | 7.68 (± 14.733) | -7.57 (± 10.124) |
| aPTT, Change at Day 113 | 8.46 (± 23.391) | 0.78 (± 16.332) | -0.97 (± 26.633) | 9.37 (± 20.265) |

Notes:

[33] - Not all subjects had data for some specific rows of time points.

[34] - Not all subjects had data for some specific rows of time points.

[35] - Not all subjects had data for some specific rows of time points.

[36] - Not all subjects had data for some specific rows of time points.

| End point values | Overall PF-06741086 300 mg SC | Total | | |
|--------------------------------------|-------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 14 ^[37] | 26 ^[38] | | |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| aPTT, Change at Day 8 | -1.89 (± 16.512) | 3.98 (± 16.079) | | |
| aPTT, Change at Day 15 | -0.38 (± 13.457) | 2.96 (± 15.825) | | |
| aPTT, Change at Day 22 | 1.51 (± 17.381) | 4.65 (± 15.543) | | |
| aPTT, Change at Day 29 | -0.74 (± 17.386) | 4.41 (± 16.009) | | |
| aPTT, Change at Day 57 | 2.26 (± 15.966) | 6.65 (± 14.817) | | |
| aPTT, Change at Day 85 | 1.35 (± 13.278) | 3.45 (± 14.257) | | |
| aPTT, Change at Day 113 | 8.88 (± 21.093) | 5.05 (± 20.500) | | |

Notes:

[37] - Not all subjects had data for some specific rows of time points.

[38] - Not all subjects had data for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline for Fibrinogen by Dose Cohort

| | |
|-----------------|--|
| End point title | Change From Baseline for Fibrinogen by Dose Cohort ^[39] |
|-----------------|--|

End point description:

Fibrinogen is a protein, specifically a clotting factor (factor I), that is essential for proper blood clot formation. Blood samples were obtained to evaluate the amount of fibrinogen.

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

End point timeframe:

Baseline, Study Day 8, 15, 22, 29, 57, 85 and 113.

Notes:

[39] - 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 planned for this endpoint

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[40] | 6 ^[41] | 6 ^[42] | 7 ^[43] |
| Units: milligram/deciliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Fibrinogen, Change at Day 8 | -49.7 (± 28.72) | -59.7 (± 38.20) | -3.5 (± 24.16) | -54.4 (± 59.58) |
| Fibrinogen, Change at Day 15 | -59.4 (± 41.28) | -51.0 (± 31.84) | -8.3 (± 25.96) | -85.6 (± 94.86) |
| Fibrinogen, Change at Day 22 | -72.0 (± 40.76) | -36.8 (± 44.93) | -33.2 (± 32.41) | -87.9 (± 115.49) |
| Fibrinogen, Change at Day 29 | -84.7 (± 43.53) | -40.0 (± 26.57) | -40.3 (± 20.99) | -99.9 (± 106.59) |
| Fibrinogen, Change at Day 57 | -33.5 (± 85.81) | 10.0 (± 79.34) | -21.3 (± 24.23) | -58.7 (± 71.81) |
| Fibrinogen, Change at Day 85 | -49.9 (± 47.93) | -39.4 (± 63.27) | -10.5 (± 44.94) | -40.8 (± 74.28) |
| Fibrinogen, Change at Day 113 | -38.6 (± 44.48) | -5.2 (± 29.34) | 23.5 (± 26.80) | -61.7 (± 126.18) |

Notes:

[40] - Not all subjects had data for some specific rows of time points.

[41] - Not all subjects had data for some specific rows of time points.

[42] - Not all subjects had data for some specific rows of time points.

[43] - Not all subjects had data for some specific rows of time points.

| End point values | Overall PF- 06741086 300 mg SC | Total | | |
|--------------------------------------|--------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 14 ^[44] | 26 ^[45] | | |
| Units: milligram/deciliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Fibrinogen, Change at Day 8 | -52.1 (± 45.00) | -42.6 (± 44.14) | | |
| Fibrinogen, Change at Day 15 | -72.5 (± 71.58) | -52.7 (± 60.78) | | |
| Fibrinogen, Change at Day 22 | -79.9 (± 83.61) | -59.2 (± 69.08) | | |
| Fibrinogen, Change at Day 29 | -92.8 (± 80.82) | -67.6 (± 65.01) | | |
| Fibrinogen, Change at Day 57 | -46.1 (± 76.57) | -25.9 (± 69.68) | | |
| Fibrinogen, Change at Day 85 | -45.7 (± 58.91) | -35.6 (± 56.31) | | |
| Fibrinogen, Change at Day 113 | -49.2 (± 88.13) | -25.1 (± 73.56) | | |

Notes:

[44] - Not all subjects had data for some specific rows of time points.

[45] - Not all subjects had data for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline for Antithrombin III by Dose Cohort

| | |
|-----------------|--|
| End point title | Change From Baseline for Antithrombin III by Dose Cohort ^[46] |
|-----------------|--|

End point description:

Antithrombin (AT) is a protein produced by the liver that helps regulate blood clot formation (i.e., a naturally-occurring mild blood thinner). Blood samples were collected to measure the activity (function) and the amount (quantity) of antithrombin in an individual's blood is used to evaluate the person for excessive blood clotting.

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

End point timeframe:

Baseline, Study Day 8, 15, 22 and 29.

Notes:

[46] - 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 planned for this endpoint

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[47] | 6 | 6 | 7 |
| Units: Percentage of activity of AT in plasma | | | | |
| arithmetic mean (standard deviation) | | | | |
| Antithrombin III, Change at Day 8 | 2.1 (± 5.18) | -1.8 (± 7.05) | 3.7 (± 7.58) | -7.3 (± 9.32) |
| Antithrombin III, Change at Day 15 | 2.4 (± 16.96) | 0.5 (± 8.14) | -15.3 (± 16.45) | -6.9 (± 6.74) |
| Antithrombin III, Change at Day 22 | -7.6 (± 17.55) | 5.2 (± 12.69) | -5.3 (± 9.97) | -4.4 (± 17.61) |
| Antithrombin III, Change at Day 29 | -0.8 (± 8.04) | -4.3 (± 11.55) | -10.3 (± 15.45) | -12.7 (± 12.96) |

Notes:

[47] - Not all subjects had data at Day 29.

| End point values | Overall PF-06741086 300 mg SC | Total | | |
|---|-------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 14 ^[48] | 26 ^[49] | | |
| Units: Percentage of activity of AT in plasma | | | | |
| arithmetic mean (standard deviation) | | | | |
| Antithrombin III, Change at Day 8 | -2.6 (± 8.74) | -1.0 (± 8.24) | | |
| Antithrombin III, Change at Day 15 | -2.2 (± 13.30) | -4.6 (± 14.02) | | |
| Antithrombin III, Change at Day 22 | -6.0 (± 16.97) | -3.3 (± 14.97) | | |
| Antithrombin III, Change at Day 29 | -7.2 (± 12.20) | -7.3 (± 12.51) | | |

Notes:

[48] - Not all subjects had data at Day 29.

[49] - Not all subjects had data at Day 29.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline for Troponin I by Dose Cohort

| | |
|--|--|
| End point title | Change From Baseline for Troponin I by Dose Cohort ^[50] |
| End point description: Blood samples were collected to measure the level of cardiac-specific troponin I in the blood to help detect heart injury. | |
| End point type | Primary |
| End point timeframe: Baseline, Study Day 22 and 29 | |

Notes:

[50] - 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 planned for this endpoint

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[51] | 6 ^[52] | 6 ^[53] | 7 ^[54] |
| Units: nanogram/milliliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Troponin I, Change at Day 22 | 0.0042 (± 0.01021) | 0 (± 0) | 0 (± 0) | 0.0142 (± 0.03470) |
| Troponin I, Change at Day 29 | 0 (± 0) | 0.0113 (± 0.02250) | 0 (± 0) | 0.0121 (± 0.03213) |

Notes:

[51] - Not all subjects had data for each row of time point.

[52] - Not all subjects had data for each row of time point.

[53] - Not all subjects had data for each row of time point.

[54] - Not all subjects had data for each row of time point.

| End point values | Overall PF-06741086 300 mg SC | Total | | |
|--------------------------------------|-------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 14 ^[55] | 26 ^[56] | | |
| Units: nanogram/milliliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Troponin I, Change at Day 22 | 0.0092 (± 0.02494) | 0.0052 (± 0.01907) | | |
| Troponin I, Change at Day 29 | 0.0065 (± 0.02357) | 0.0059 (± 0.02010) | | |

Notes:

[55] - Not all subjects had data for each row of time point.

[56] - Not all subjects had data for each row of time point.

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 ^[57] |
|-----------------|---|

End point description:

Criteria for potentially clinically important findings in vital signs data were defined as: 1) supine systolic blood pressure (BP): value <90 mm Hg or change ≥30 mm Hg increase; 2) Supine diastolic BP: value <50 mm Hg or change ≥20 mm Hg increase; 3) Supine pulse rate: value <40 beats/min or >120

beats/min.

| | |
|---------------------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| Baseline to Study Day 113 Visit | |

Notes:

[57] - 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 planned for this endpoint

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 6 | 7 |
| Units: Subjects | | | | |
| Supine systolic BP value <90 mm Hg | 0 | 0 | 0 | 0 |
| Supine systolic BP change \geq 30 mm Hg increase | 0 | 1 | 1 | 0 |
| Supine diastolic BP value <50 mm Hg | 0 | 0 | 0 | 0 |
| Supine diastolic BP change \geq 20 mm Hg increase | 0 | 1 | 0 | 0 |
| Supine pulse rate value <40 beats/min | 0 | 0 | 0 | 0 |
| Supine pulse rate value >120 beats/min | 0 | 0 | 0 | 0 |

| End point values | Overall PF- 06741086 300 mg SC | Total | | |
|---|--------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 14 | 26 | | |
| Units: Subjects | | | | |
| Supine systolic BP value <90 mm Hg | 0 | 0 | | |
| Supine systolic BP change \geq 30 mm Hg increase | 0 | 2 | | |
| Supine diastolic BP value <50 mm Hg | 0 | 0 | | |
| Supine diastolic BP change \geq 20 mm Hg increase | 0 | 1 | | |
| Supine pulse rate value <40 beats/min | 0 | 0 | | |
| Supine pulse rate value >120 beats/min | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Electrocardiogram (ECG) Change Meeting Pre-specified Criteria

| | |
|-----------------|---|
| End point title | Number of Subjects With Electrocardiogram (ECG) Change Meeting Pre-specified Criteria ^[58] |
|-----------------|---|

End point description:

Criteria for potentially clinically important changes in ECG were defined as: PR interval baseline >200 msec and increase of $\geq 25\%$; PR interval baseline ≤ 200 msec and increase of $\geq 50\%$; QRS interval increase of $\geq 50\%$. Only the number of subjects meeting pre-defined criteria was reported below.

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

End point timeframe:

Baseline to Study Day 29 Visit.

Notes:

[58] - 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 planned for this endpoint

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|-----------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 6 | 7 |
| Units: Subjects | 0 | 0 | 0 | 0 |

| End point values | Overall PF- 06741086 300 mg SC | Total | | |
|-----------------------------|--------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 14 | 26 | | |
| Units: Subjects | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Changes in Physical Examination Findings

| | |
|-----------------|---|
| End point title | Number of Subjects With Clinically Significant Changes in Physical Examination Findings ^[59] |
|-----------------|---|

End point description:

Physical examination included head, ears, eyes, nose, mouth, skin, heart and lung examinations, lymph nodes, gastrointestinal, musculoskeletal, and neurological systems. Clinical significance was judged by the investigator.

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

End point timeframe:

Baseline to Study Day 113 Visit

Notes:

[59] - 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 planned for this endpoint

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|-----------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 6 | 7 |
| Units: Subjects | 0 | 0 | 0 | 0 |

| End point values | Overall PF- 06741086 300 mg SC | Total | | |
|-----------------------------|--------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 14 | 26 | | |
| Units: Subjects | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Infusion and Injection Site Reactions

| | |
|-----------------|---|
| End point title | Number of Subjects With Infusion and Injection Site |
|-----------------|---|

End point description:

Infusion and injection site reactions included: injection site bruising, injection site erythema, injection site haemorrhage, injection site induration, injection site pain, injection site pruritus, injection site swelling and injection site warmth. Grade of severity was defined as follows: Mild: Transient or mild discomfort (< 48 hours); no medical intervention/therapy required. Moderate: Mild to moderate limitation in activity - some assistance may be needed; no or minimal medical intervention/therapy required. Severe: Marked limitation in activity, some assistance usually required; medical intervention/therapy required, hospitalizations possible.

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

End point timeframe:

Baseline to Study Day 113 Visit

Notes:

[60] - 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 planned for this endpoint

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|-----------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 6 | 7 |
| Units: Subjects | | | | |
| All-causality Mild | 3 | 1 | 0 | 1 |
| Treatment-related Mild | 3 | 1 | 0 | 1 |
| All-causality Moderate | 0 | 0 | 0 | 1 |
| Treatment-related Moderate | 0 | 0 | 0 | 1 |
| All-causality Severe | 0 | 0 | 2 | 0 |

| | | | | |
|--------------------------|---|---|---|---|
| Treatment-related Severe | 0 | 0 | 2 | 0 |
|--------------------------|---|---|---|---|

| End point values | Overall PF-06741086 300 mg SC | Total | | |
|-----------------------------|-------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 14 | 26 | | |
| Units: Subjects | | | | |
| All-causality Mild | 4 | 5 | | |
| Treatment-related Mild | 4 | 5 | | |
| All-causality Moderate | 1 | 1 | | |
| Treatment-related Moderate | 1 | 1 | | |
| All-causality Severe | 0 | 2 | | |
| Treatment-related Severe | 0 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Bleeding Rate (ABR)

| | |
|-----------------|--------------------------------|
| End point title | Annualized Bleeding Rate (ABR) |
|-----------------|--------------------------------|

End point description:

Pre-treatment ABR = number of bleeding episodes within 6 months prior to study enrollment (total number of bleeding episodes in hemophilia history CRF) × 2; On-study ABR = number of bleeding episodes occurred within 9 days after the last dose / ([last dose date + 9 - first dose date + 1] / 365.25)

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

End point timeframe:

Pre-treatment: within 6 months prior to study enrollment; On-study: Day 1 to 9 days after the last dose (Day 78)

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|--------------------------------------|--|--|--|------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 6 | 6 | 6 |
| Units: Bleeding episodes per year | | | | |
| arithmetic mean (standard deviation) | | | | |
| Pre-Treatment | 23.00 (± 7.457) | 14.67 (± 1.633) | 20.33 (± 10.838) | 17.33 (± 3.011) |
| On-Study | 4.22 (± 3.799) | 1.62 (± 2.533) | 4.17 (± 6.467) | 0.65 (± 1.603) |

| End point values | Overall PF-06741086 300 mg SC | Total | | |
|--------------------------------------|-------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 12 | 24 | | |
| Units: Bleeding episodes per year | | | | |
| arithmetic mean (standard deviation) | | | | |
| Pre-Treatment | 20.17 (± 6.177) | 18.83 (± 7.100) | | |
| On-Study | 2.43 (± 3.345) | 2.67 (± 4.092) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma PF-06741086 concentrations

| | |
|---|-----------------------------------|
| End point title | Plasma PF-06741086 concentrations |
| End point description: Plasma PF-06741086 concentrations were analyzed using a validated, sensitive and specific electrochemiluminescence (ECL) method. Not all subjects had data at each visit. | |
| End point type | Secondary |
| End point timeframe: pre-dose on Study Day 1, 24hours (h), 72h post Study Day 1 dosing, pre-dose on Study Day 8, 15 and 22, pre-dose on Study Day 29, 24h, 96h post Study Day 29 dosing, pre-dose on Study Day 57, 168h, 840h post Study Day 57 dosing | |

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|--------------------------------------|--|--|--|------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[61] | 6 ^[62] | 6 ^[63] | 7 ^[64] |
| Units: nanogram/milliliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Pre-dose on Day 1 | 99999 (± 99999) | 99999 (± 99999) | 99999 (± 99999) | 99999 (± 99999) |
| 24h post Day 1 dosing | 12180 (± 8500.2) | 15620 (± 8055.3) | 11640 (± 4670.6) | 18130 (± 9111.3) |
| 72h post Day 1 dosing | 17560 (± 10637) | 20850 (± 8433.7) | 24270 (± 8018.9) | 20640 (± 8978.4) |
| Pre-dose on Day 8 | 11290 (± 10019) | 14060 (± 6201.2) | 16700 (± 5689.1) | 11940 (± 4981.7) |
| Pre-dose on Day 15 | 22850 (± 15142) | 16680 (± 7668.8) | 28180 (± 10163) | 24870 (± 5726.8) |
| Pre-dose on Day 22 | 33010 (± 19724) | 17900 (± 10509) | 41200 (± 17504) | 36450 (± 10432) |
| Pre-dose on Day 29 | 46180 (± 21357) | 16780 (± 7939.7) | 59950 (± 30625) | 41500 (± 13884) |
| 24h post Day 29 dosing | 66500 (± 27135) | 23530 (± 8548.4) | 73780 (± 22425) | 69920 (± 27902) |

| | | | | |
|-------------------------|------------------|------------------|-----------------|------------------|
| 96h post Day 29 dosing | 69130 (± 30459) | 20680 (± 11580) | 74950 (± 27538) | 58150 (± 18753) |
| Pre-dose on Day 57 | 54580 (± 29022) | 18260 (± 15062) | 66480 (± 45529) | 59140 (± 24377) |
| 168h post Day 57 dosing | 53890 (± 43483) | 24800 (± 2994.4) | 87500 (± 37163) | 66700 (± 28971) |
| 840h post Day 57 dosing | 586.6 (± 1318.4) | 99999 (± 99999) | 99999 (± 99999) | 90.00 (± 180.00) |

Notes:

[61] - Not all subjects had data for some specific rows of time points.

[62] - Not all subjects had data for some specific rows of time points.

[63] - Not all subjects had data for some specific rows of time points.

[64] - Not all subjects had data for some specific rows of time points.

| | | | | |
|--------------------------------------|-------------------------------|--|--|--|
| End point values | Overall PF-06741086 300 mg SC | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 14 ^[65] | | | |
| Units: nanogram/milliliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Pre-dose on Day 1 | 99999 (± 99999) | | | |
| 24h post Day 1 dosing | 15150 (± 9011.0) | | | |
| 72h post Day 1 dosing | 19100 (± 9591.3) | | | |
| Pre-dose on Day 8 | 11610 (± 7609.2) | | | |
| Pre-dose on Day 15 | 23860 (± 11048) | | | |
| Pre-dose on Day 22 | 34600 (± 15590) | | | |
| Pre-dose on Day 29 | 43840 (± 17161) | | | |
| 24h post Day 29 dosing | 68210 (± 26010) | | | |
| 96h post Day 29 dosing | 62860 (± 22794) | | | |
| Pre-dose on Day 57 | 56860 (± 25382) | | | |
| 168h post Day 57 dosing | 60300 (± 35481) | | | |
| 840h post Day 57 dosing | 406.0 (± 1056.1) | | | |

Notes:

[65] - Not all subjects had data for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-time Profile From Time Zero to the Time of the Last Quantifiable Concentration (AUClast) of PF-06741086

| | |
|-----------------|--|
| End point title | Area Under the Concentration-time Profile From Time Zero to the Time of the Last Quantifiable Concentration (AUClast) of PF-06741086 |
|-----------------|--|

End point description:

AUClast was calculated by linear/Log trapezoidal method.

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

End point timeframe:

Pre-dose on Day 1, 24 and 96 hours post Day 1 dosing

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 6 | 7 |
| Units: nanogram*hour/milliliter | | | | |
| geometric mean (geometric coefficient of variation) | 1818000 (\pm 79) | 2675000 (\pm 41) | 2806000 (\pm 37) | 2495000 (\pm 40) |

| End point values | Overall PF- 06741086 300 mg SC | | | |
|---|--------------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 14 | | | |
| Units: nanogram*hour/milliliter | | | | |
| geometric mean (geometric coefficient of variation) | 2130000 (\pm 61) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (Cmax) of PF-06741086

| | |
|-----------------|--|
| End point title | Maximum Plasma Concentration (Cmax) of PF-06741086 |
|-----------------|--|

End point description:

Cmax was observed directly from data. Not all subjects had data at Day 29.

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

End point timeframe:

Pre-dose on Day 1, 24 and 96 hours post Day 1 dosing, pre-dose on Day 29, 24 and 96 hours post Day 29 dosing

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[66] | 6 | 6 ^[67] | 7 ^[68] |
| Units: nanogram/milliliter | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| C _{max} , Day 1 | 14880 (± 70) | 19480 (± 42) | 23070 (± 37) | 19680 (± 51) |
| C _{max} , Day 29 | 61850 (± 47) | 24150 (± 44) | 73490 (± 38) | 66070 (± 44) |

Notes:

[66] - Not all subjects had data for some specific time points.

[67] - Not all subjects had data for some specific time points.

[68] - Not all subjects had data for some specific time points.

| End point values | Overall PF- 06741086 300 mg SC | | | |
|---|--------------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 14 ^[69] | | | |
| Units: nanogram/milliliter | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| C _{max} , Day 1 | 17110 (± 61) | | | |
| C _{max} , Day 29 | 63930 (± 43) | | | |

Notes:

[69] - Not all subjects had data for some specific time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Lowest Concentration Observed During the Dosing Interval (C_{min}) of PF-06741086

| | |
|------------------------|---|
| End point title | Lowest Concentration Observed During the Dosing Interval (C _{min}) of PF-06741086 |
| End point description: | C _{min} was observed directly from data. Not all subjects had data at Day 29. |
| End point type | Secondary |
| End point timeframe: | Post-dose on Day 2 (-6 hours/+1 day), Day 4 (-6 hours/+1 day), Day 30 (-6 hours/+1 day) and Day 33 (-6 hours/+1 day). |

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|-----------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[70] | 6 | 6 ^[71] | 7 ^[72] |
| Units: nanogram/milliliter | | | | |

| | | | | |
|---|--------------|--------------|--------------|--------------|
| geometric mean (geometric coefficient of variation) | | | | |
| Cmin, Day 1 | 7980 (± 112) | 13040 (± 43) | 15660 (± 44) | 11140 (± 41) |
| Cmin, Day 29 | 42120 (± 52) | 15000 (± 59) | 53630 (± 61) | 39490 (± 37) |

Notes:

[70] - Not all subjects had data for some specific time points.

[71] - Not all subjects had data for some specific time points.

[72] - Not all subjects had data for some specific time points.

| | | | | |
|---|-------------------------------|--|--|--|
| End point values | Overall PF-06741086 300 mg SC | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 14 ^[73] | | | |
| Units: nanogram/milliliter | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cmin, Day 1 | 9429 (± 78) | | | |
| Cmin, Day 29 | 40790 (± 42) | | | |

Notes:

[73] - Not all subjects had data for some specific time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Plasma Concentration (Tmax) of PF-06741086

| | |
|-----------------|--|
| End point title | Time to Reach Maximum Plasma Concentration (Tmax) of PF-06741086 |
|-----------------|--|

End point description:

Tmax was observed directly from data as time of first occurrence. Not all subjects had data at Day 29.

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

End point timeframe:

Pre-dose on Day 1, 24 and 96 hours post Day 1 dosing, pre-dose on Day 29, 24 and 96 hours post Day 29 dosing

| | | | | |
|-------------------------------|--|--|--|------------------------------------|
| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[74] | 6 | 6 ^[75] | 7 ^[76] |
| Units: hours | | | | |
| median (full range (min-max)) | | | | |
| Tmax, Day 1 | 70.0 (69.1 to 72.8) | 69.7 (68.2 to 71.1) | 71.6 (67.6 to 72.3) | 70.7 (22.8 to 167) |
| Tmax, Day 29 | 23.7 (23.1 to 94.2) | 23.7 (22.0 to 71.7) | 58.5 (23.3 to 97.0) | 22.8 (22.1 to 94.7) |

Notes:

[74] - Not all subjects had data for some specific time points.

[75] - Not all subjects had data for some specific time points.

[76] - Not all subjects had data for some specific time points.

| | | | | |
|-------------------------------|-------------------------------|--|--|--|
| End point values | Overall PF-06741086 300 mg SC | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 14 ^[77] | | | |
| Units: hours | | | | |
| median (full range (min-max)) | | | | |
| Tmax, Day 1 | 70.1 (22.8 to 167) | | | |
| Tmax, Day 29 | 23.3 (22.1 to 94.7) | | | |

Notes:

[77] - Not all subjects had data for some specific time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Serum Concentration-time Curve Over the Dosing Interval tau (AUCtau) of PF-06741086

| | |
|------------------------|--|
| End point title | Area Under the Serum Concentration-time Curve Over the Dosing Interval tau (AUCtau) of PF-06741086 |
| End point description: | The dosing interval tau was 1 week. AUCtau was obtained by linear/log trapezoidal method. |
| End point type | Secondary |
| End point timeframe: | Pre-dose on Day 29, 24 and 96 hours post Day 29 dosing |

| | | | | |
|---|--|--|--|------------------------------------|
| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 6 | 4 | 5 |
| Units: nanogram*hour/milliliter | | | | |
| geometric mean (geometric coefficient of variation) | 9045000 (\pm 49) | 3309000 (\pm 50) | 11090000 (\pm 43) | 9248000 (\pm 38) |

| | | | | |
|---|-------------------------------|--|--|--|
| End point values | Overall PF-06741086 300 mg SC | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 10 | | | |
| Units: nanogram*hour/milliliter | | | | |
| geometric mean (geometric coefficient of variation) | 9146000 (\pm) | | | |

| | |
|---------------|-----|
| of variation) | 41) |
|---------------|-----|

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Clearance After Oral Dose (CL/F) of PF-06741086

| | |
|--|--|
| End point title | Apparent Clearance After Oral Dose (CL/F) of PF-06741086 |
| End point description: CL/F was calculated by dose/AUCtau. | |
| End point type | Secondary |
| End point timeframe: Pre-dose on Day 29, 24 and 96 hours post Day 29 dosing | |

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 6 | 4 | 5 |
| Units: milliliter/hour | | | | |
| geometric mean (geometric coefficient of variation) | 33.16 (± 49) | 45.34 (± 50) | 40.60 (± 43) | 32.43 (± 38) |

| End point values | Overall PF- 06741086 300 mg SC | | | |
|---|--------------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 10 | | | |
| Units: milliliter/hour | | | | |
| geometric mean (geometric coefficient of variation) | 32.79 (± 41) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Tissue Factor Pathway Inhibitor (TFPI)

| | |
|-----------------|--|
| End point title | Change From Baseline in Total Tissue Factor Pathway Inhibitor (TFPI) |
|-----------------|--|

End point description:

Total amount of tissue factor pathway inhibitor (TFPI) (bound and unbound) in plasma. TFPI is a protease inhibitor which acts as an antagonist of the extrinsic coagulation pathway via inhibition of tissue factor activated coagulation factor VII (FVIIa) and activated factor X (FXa). Human plasma samples were analyzed for total TFPI concentrations using a validated, sensitive and specific high-performance liquid chromatography tandem mass spectrometric method (LC-MS/MS). Mixed model repeated measures (MMRM) was used to analyze the change from baseline on TFPI.

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

End point timeframe:

Baseline, Study Day 2, 4, 8, 15, 22, 29, 30, 33, 57, 85 and 113

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[78] | 6 ^[79] | 6 ^[80] | 7 ^[81] |
| Units: nanogram/milliliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| TFPI, Change at Day 2 | 3.9 (± 31.43) | -13.4 (± 17.17) | 8.2 (± 19.83) | 0.4 (± 46.81) |
| TFPI, Change at Day 4 | 39.4 (± 46.10) | 43.2 (± 25.76) | 74.0 (± 22.03) | 86.0 (± 29.71) |
| TFPI, Change at Day 8 | 42.7 (± 82.52) | 72.4 (± 10.81) | 120.5 (± 34.41) | 55.9 (± 69.84) |
| TFPI, Change at Day 15 | 143.9 (± 107.56) | 78.8 (± 43.36) | 186.5 (± 52.80) | 156.1 (± 83.87) |
| TFPI, Change at Day 22 | 256.1 (± 137.09) | 110.0 (± 80.96) | 301.5 (± 84.39) | 223.3 (± 128.08) |
| TFPI, Change at Day 29 | 324.2 (± 127.46) | 106.6 (± 77.56) | 334.7 (± 120.67) | 222.1 (± 135.29) |
| TFPI, Change at Day 30 | 363.8 (± 156.87) | 115.6 (± 86.41) | 347.8 (± 170.70) | 286.7 (± 103.72) |
| TFPI, Change at Day 33 | 337.7 (± 129.05) | 165.8 (± 35.20) | 351.0 (± 161.54) | 296.3 (± 112.30) |
| TFPI, Change at Day 57 | 383.3 (± 137.17) | 140.0 (± 126.96) | 460.5 (± 247.37) | 371.0 (± 178.73) |
| TFPI, Change at Day 85 | 396.7 (± 216.54) | 246.7 (± 51.81) | 492.2 (± 308.46) | 425.0 (± 266.57) |
| TFPI, Change at Day 113 | 30.0 (± 72.30) | 41.5 (± 28.99) | 39.0 (± 16.15) | -14.0 (± 33.17) |

Notes:

[78] - Number of subjects analyzed was 6 at Day 29.

[79] - Not all subjects were analyzed for some specific rows of time points.

[80] - Not all subjects were analyzed for some specific rows of time points.

[81] - Not all subjects were analyzed for some specific rows of time points.

| End point values | Overall PF- 06741086 300 mg SC | | | |
|--------------------------------------|--------------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 14 ^[82] | | | |
| Units: nanogram/milliliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| TFPI, Change at Day 2 | 2.1 (± 38.35) | | | |

| | | | | |
|-------------------------|------------------|--|--|--|
| TFPI, Change at Day 4 | 62.7 (± 44.41) | | | |
| TFPI, Change at Day 8 | 49.3 (± 73.76) | | | |
| TFPI, Change at Day 15 | 150.0 (± 92.88) | | | |
| TFPI, Change at Day 22 | 239.7 (± 128.59) | | | |
| TFPI, Change at Day 29 | 269.2 (± 136.83) | | | |
| TFPI, Change at Day 30 | 325.3 (± 133.04) | | | |
| TFPI, Change at Day 33 | 317.0 (± 117.34) | | | |
| TFPI, Change at Day 57 | 377.2 (± 152.03) | | | |
| TFPI, Change at Day 85 | 409.8 (± 230.80) | | | |
| TFPI, Change at Day 113 | 9.7 (± 59.94) | | | |

Notes:

[82] - Not all subjects were analyzed for some specific rows of time points

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Thrombin Generation (TGA) Lag Time

| | |
|-----------------|--|
| End point title | Change From Baseline in Thrombin Generation (TGA) Lag Time |
|-----------------|--|

End point description:

An ex vivo pharmacodynamic measure of thrombin generation (initiation of thrombin generation), the lag time is the time needed to form the first traces of thrombin.

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

End point timeframe:

Baseline, Study Day 2, 4, 8, 15, 22, 29, 30, 33, 57, 85 and 113

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[83] | 6 ^[84] | 6 ^[85] | 7 ^[86] |
| Units: minutes | | | | |
| arithmetic mean (standard deviation) | | | | |
| TGA lag time, Change at Day 2 | -7.16 (± 5.865) | -2.77 (± 1.517) | -3.93 (± 1.919) | -4.13 (± 1.238) |
| TGA lag time, Change at Day 4 | -6.80 (± 6.079) | -2.80 (± 1.399) | -3.48 (± 1.957) | -4.17 (± 1.501) |
| TGA lag time, Change at Day 8 | -6.94 (± 5.882) | -2.88 (± 1.292) | -3.57 (± 2.018) | -4.43 (± 1.506) |
| TGA lag time, Change at Day 15 | -6.90 (± 5.897) | -3.07 (± 1.221) | -3.27 (± 1.870) | -4.29 (± 1.342) |
| TGA lag time, Change at Day 22 | -6.94 (± 5.978) | -2.80 (± 1.585) | -3.12 (± 2.097) | -4.34 (± 1.638) |
| TGA lag time, Change at Day 29 | -5.33 (± 4.871) | -2.77 (± 1.392) | -3.43 (± 2.016) | -4.32 (± 1.781) |

| | | | | |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| TGA lag time, Change at Day 30 | -5.22 (± 4.893) | -2.77 (± 1.372) | -3.50 (± 2.082) | -4.48 (± 1.681) |
| TGA lag time, Change at Day 33 | -5.08 (± 4.414) | -2.40 (± 1.568) | -3.35 (± 2.261) | -4.52 (± 1.771) |
| TGA lag time, Change at Day 57 | -4.73 (± 4.711) | -2.28 (± 2.020) | -3.42 (± 1.962) | -3.78 (± 1.376) |
| TGA lag time, Change at Day 85 | -6.34 (± 5.745) | -3.10 (± 1.344) | -3.27 (± 2.014) | -3.33 (± 1.755) |
| TGA lag time, Change at Day 113 | -0.79 (± 7.428) | 0.80 (± 0.283) | 1.53 (± 5.306) | 0.78 (± 5.251) |

Notes:

[83] - Not all subjects were analyzed for some specific rows of time points.

[84] - Not all subjects were analyzed for some specific rows of time points.

[85] - Not all subjects were analyzed for some specific rows of time points.

[86] - Not all subjects were analyzed for some specific rows of time points.

| End point values | Overall PF-06741086 300 mg SC | | | |
|--------------------------------------|-------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 14 ^[87] | | | |
| Units: minutes | | | | |
| arithmetic mean (standard deviation) | | | | |
| TGA lag time, Change at Day 2 | -5.64 (± 4.365) | | | |
| TGA lag time, Change at Day 4 | -5.49 (± 4.467) | | | |
| TGA lag time, Change at Day 8 | -5.69 (± 4.327) | | | |
| TGA lag time, Change at Day 15 | -5.59 (± 4.327) | | | |
| TGA lag time, Change at Day 22 | -5.64 (± 4.422) | | | |
| TGA lag time, Change at Day 29 | -4.83 (± 3.537) | | | |
| TGA lag time, Change at Day 30 | -4.88 (± 3.640) | | | |
| TGA lag time, Change at Day 33 | -4.83 (± 3.329) | | | |
| TGA lag time, Change at Day 57 | -4.26 (± 3.346) | | | |
| TGA lag time, Change at Day 85 | -4.95 (± 4.497) | | | |
| TGA lag time, Change at Day 113 | -0.06 (± 6.304) | | | |

Notes:

[87] - Not all subjects were analyzed for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Thrombin Generation (TGA) Peak

| | |
|-----------------|--|
| End point title | Change From Baseline in Thrombin Generation (TGA) Peak |
|-----------------|--|

End point description:

An ex vivo pharmacodynamic measure of thrombin generation (initiation of thrombin generation). The peak represents the highest thrombin concentration that can be generated. There may be patients who reach the peak faster or slower than others and this may represent hyper- or hypocoagulability,

respectively.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Study Day 2, 4, 8, 15, 22, 29, 30, 33, 57, 85 and 113 | |

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[88] | 6 ^[89] | 6 ^[90] | 7 ^[91] |
| Units: nanomole | | | | |
| arithmetic mean (standard deviation) | | | | |
| TGA peak, Change at Day 2 | 72.93 (± 35.734) | 70.92 (± 23.721) | 68.18 (± 15.693) | 63.41 (± 9.743) |
| TGA peak, Change at Day 4 | 60.00 (± 30.196) | 59.28 (± 30.156) | 50.87 (± 20.687) | 51.79 (± 14.929) |
| TGA peak, Change at Day 8 | 49.36 (± 32.033) | 56.00 (± 33.636) | 50.30 (± 14.019) | 54.36 (± 15.007) |
| TGA peak, Change at Day 15 | 49.01 (± 23.471) | 52.57 (± 28.440) | 46.40 (± 22.985) | 40.90 (± 7.886) |
| TGA peak, Change at Day 22 | 44.50 (± 27.260) | 52.07 (± 33.558) | 38.15 (± 16.313) | 44.41 (± 22.567) |
| TGA peak, Change at Day 29 | 42.95 (± 24.026) | 49.72 (± 29.316) | 38.23 (± 21.808) | 42.48 (± 23.057) |
| TGA peak, Change at Day 30 | 35.93 (± 26.177) | 51.75 (± 29.276) | 37.72 (± 24.136) | 48.62 (± 21.427) |
| TGA peak, Change at Day 33 | 76.68 (± 69.887) | 46.83 (± 37.084) | 36.25 (± 21.955) | 54.10 (± 28.276) |
| TGA peak, Change at Day 57 | 37.13 (± 21.866) | 32.57 (± 20.368) | 34.67 (± 20.584) | 33.93 (± 7.688) |
| TGA peak, Change at Day 85 | 37.60 (± 21.142) | 69.92 (± 40.250) | 30.15 (± 18.614) | 30.15 (± 22.743) |
| TGA peak, Change at Day 113 | 24.37 (± 33.703) | 16.05 (± 36.557) | 43.33 (± 68.794) | 6.93 (± 15.334) |

Notes:

[88] - Not all subjects were analyzed for some specific rows of time points.

[89] - Not all subjects were analyzed for some specific rows of time points.

[90] - Not all subjects were analyzed for some specific rows of time points.

[91] - Not all subjects were analyzed for some specific rows of time points.

| End point values | Overall PF- 06741086 300 mg SC | | | |
|--------------------------------------|--------------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 14 ^[92] | | | |
| Units: nanomole | | | | |
| arithmetic mean (standard deviation) | | | | |
| TGA peak, Change at Day 2 | 68.17 (± 25.642) | | | |
| TGA peak, Change at Day 4 | 55.89 (± 23.278) | | | |
| TGA peak, Change at Day 8 | 51.86 (± 24.171) | | | |

| | | | | |
|-----------------------------|------------------|--|--|--|
| TGA peak, Change at Day 15 | 44.96 (± 17.340) | | | |
| TGA peak, Change at Day 22 | 44.46 (± 24.042) | | | |
| TGA peak, Change at Day 29 | 42.72 (± 22.452) | | | |
| TGA peak, Change at Day 30 | 41.70 (± 23.878) | | | |
| TGA peak, Change at Day 33 | 66.42 (± 53.861) | | | |
| TGA peak, Change at Day 57 | 35.53 (± 15.716) | | | |
| TGA peak, Change at Day 85 | 34.16 (± 21.306) | | | |
| TGA peak, Change at Day 113 | 16.32 (± 27.345) | | | |

Notes:

[92] - Not all subjects were analyzed for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Endogenous Thrombin Generation (TGA) Potential

| | |
|-----------------|--|
| End point title | Change From Baseline in Endogenous Thrombin Generation (TGA) Potential |
|-----------------|--|

End point description:

An ex vivo pharmacodynamic measure of thrombin generation. The endogenous TGA potential represents the total amount of active thrombin formed during thrombin generation and the peak height the maximal amount of thrombin formed.

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

End point timeframe:

Baseline, Study Day 2, 4, 8, 15, 22, 29, 30, 33, 57, 85 and 113

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[93] | 6 ^[94] | 6 ^[95] | 7 ^[96] |
| Units: nanomole*minute | | | | |
| arithmetic mean (standard deviation) | | | | |
| Endogenous TGA Potential, Change at Day 2 | 864.0 (± 250.60) | 816.8 (± 211.13) | 999.8 (± 249.59) | 1065.3 (± 161.71) |
| Endogenous TGA Potential, Change at Day 4 | 766.7 (± 236.94) | 714.8 (± 275.75) | 808.7 (± 288.78) | 825.1 (± 294.44) |
| Endogenous TGA Potential, Change at Day 8 | 691.9 (± 301.43) | 659.8 (± 295.11) | 796.5 (± 151.00) | 918.6 (± 276.26) |
| Endogenous TGA Potential, Change at Day 15 | 674.9 (± 244.61) | 608.5 (± 242.81) | 800.8 (± 334.99) | 639.3 (± 145.74) |
| Endogenous TGA Potential, Change at Day 22 | 646.9 (± 295.05) | 589.0 (± 274.33) | 647.0 (± 236.38) | 731.4 (± 302.89) |

| | | | | |
|---|------------------|------------------|------------------|------------------|
| Endogenous TGA Potential, Change at Day 29 | 588.2 (± 239.00) | 623.0 (± 188.84) | 618.3 (± 276.51) | 660.5 (± 340.36) |
| Endogenous TGA Potential, Change at Day 30 | 494.8 (± 247.86) | 672.0 (± 226.25) | 603.3 (± 332.44) | 710.2 (± 272.54) |
| Endogenous TGA Potential, Change at Day 33 | 716.5 (± 391.60) | 606.0 (± 280.39) | 583.7 (± 291.25) | 848.8 (± 387.17) |
| Endogenous TGA Potential, Change at Day 57 | 586.8 (± 200.04) | 445.2 (± 220.86) | 564.5 (± 287.43) | 579.7 (± 147.04) |
| Endogenous TGA Potential, Change at Day 85 | 566.6 (± 202.22) | 812.2 (± 198.80) | 526.7 (± 297.03) | 493.7 (± 368.68) |
| Endogenous TGA Potential, Change at Day 113 | 256.4 (± 347.91) | 50.5 (± 290.62) | 306.5 (± 440.04) | 142.3 (± 361.25) |

Notes:

[93] - Not all subjects were analyzed for some specific rows of time points.

[94] - Not all subjects were analyzed for some specific rows of time points.

[95] - Not all subjects were analyzed for some specific rows of time points.

[96] - Not all subjects were analyzed for some specific rows of time points.

| | | | | |
|---|-------------------------------|--|--|--|
| End point values | Overall PF-06741086 300 mg SC | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 14 ^[97] | | | |
| Units: nanomole*minute | | | | |
| arithmetic mean (standard deviation) | | | | |
| Endogenous TGA Potential, Change at Day 2 | 964.6 (± 227.95) | | | |
| Endogenous TGA Potential, Change at Day 4 | 795.9 (± 258.54) | | | |
| Endogenous TGA Potential, Change at Day 8 | 805.2 (± 301.66) | | | |
| Endogenous TGA Potential, Change at Day 15 | 657.1 (± 194.32) | | | |
| Endogenous TGA Potential, Change at Day 22 | 689.1 (± 290.60) | | | |
| Endogenous TGA Potential, Change at Day 29 | 624.3 (± 282.93) | | | |
| Endogenous TGA Potential, Change at Day 30 | 592.7 (± 270.33) | | | |
| Endogenous TGA Potential, Change at Day 33 | 776.6 (± 376.05) | | | |
| Endogenous TGA Potential, Change at Day 57 | 583.3 (± 167.42) | | | |
| Endogenous TGA Potential, Change at Day 85 | 532.9 (± 280.20) | | | |
| Endogenous TGA Potential, Change at Day 113 | 203.8 (± 344.10) | | | |

Notes:

[97] - Not all subjects were analyzed for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Prothrombin Fragments 1 + 2

| | |
|-----------------|---|
| End point title | Change From Baseline in Prothrombin Fragments 1 + 2 |
|-----------------|---|

End point description:

An in vivo pharmacodynamic measure of thrombin generation (prothrombin cleavage). Prothrombin fragment 1+2 (F 1+2) is the amino terminus fragment of the prothrombin molecule. It is a polypeptide with a half-life of approximately 90 minutes. F 1+2 is released from prothrombin when prothrombin is converted to thrombin by the prothrombinase complex.

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

End point timeframe:

Baseline, Study Day 2, 4, 8, 15, 22, 29, 30, 33, 57, 85 and 113

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[98] | 6 ^[99] | 6 ^[100] | 7 ^[101] |
| Units: picomole/liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Prothrombin fragments 1 + 2, Change at Day 2 | 430.0 (± 383.03) | 498.3 (± 484.40) | 275.7 (± 206.71) | 438.9 (± 507.68) |
| Prothrombin fragments 1 + 2, Change at Day 4 | 548.1 (± 455.67) | 1096.7 (± 1403.57) | 574.5 (± 363.37) | 730.3 (± 537.21) |
| Prothrombin fragments 1 + 2, Change at Day 8 | 450.3 (± 396.09) | 562.2 (± 605.07) | 413.0 (± 171.50) | 580.7 (± 259.63) |
| Prothrombin fragments 1 + 2, Change at Day 15 | 481.7 (± 330.26) | 349.7 (± 212.59) | 389.2 (± 228.56) | 571.1 (± 474.23) |
| Prothrombin fragments 1 + 2, Change at Day 22 | 608.1 (± 336.97) | 322.3 (± 161.76) | 420.2 (± 166.66) | 524.1 (± 577.08) |
| Prothrombin fragments 1 + 2, Change at Day 29 | 650.3 (± 415.58) | 288.0 (± 259.19) | 577.7 (± 302.76) | 429.3 (± 257.91) |
| Prothrombin fragments 1 + 2, Change at Day 30 | 655.7 (± 496.35) | 486.0 (± 608.26) | 521.0 (± 165.25) | 580.8 (± 507.83) |
| Prothrombin fragments 1 + 2, Change at Day 33 | 761.3 (± 509.02) | 642.5 (± 759.02) | 1527.7 (± 2499.96) | 609.2 (± 380.74) |
| Prothrombin fragments 1 + 2, Change at Day 57 | 586.5 (± 473.53) | 216.5 (± 173.44) | 465.3 (± 300.84) | 463.5 (± 397.57) |
| Prothrombin fragments 1 + 2, Change at Day 85 | 588.3 (± 483.80) | 378.2 (± 207.16) | 470.2 (± 244.21) | 362.2 (± 378.54) |
| Prothrombin fragments 1 + 2, Change at Day 113 | -6.6 (± 151.87) | 16.5 (± 19.09) | -75.5 (± 76.86) | -58.2 (± 121.15) |

Notes:

[98] - Not all subjects were analyzed for some specific rows of time points.

[99] - Not all subjects were analyzed for some specific rows of time points.

[100] - Not all subjects were analyzed for some specific rows of time points.

[101] - Not all subjects were analyzed for some specific rows of time points.

| End point values | Overall PF-06741086 300 mg SC | | | |
|--|-------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 14 ^[102] | | | |
| Units: picomole/liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Prothrombin fragments 1 + 2, Change at Day 2 | 434.4 (± 432.08) | | | |

| | | | | |
|--|------------------|--|--|--|
| Prothrombin fragments 1 + 2, Change at Day 4 | 639.2 (± 487.82) | | | |
| Prothrombin fragments 1 + 2, Change at Day 8 | 515.5 (± 328.78) | | | |
| Prothrombin fragments 1 + 2, Change at Day 15 | 526.4 (± 395.34) | | | |
| Prothrombin fragments 1 + 2, Change at Day 22 | 566.1 (± 456.08) | | | |
| Prothrombin fragments 1 + 2, Change at Day 29 | 531.3 (± 344.06) | | | |
| Prothrombin fragments 1 + 2, Change at Day 30 | 618.3 (± 480.35) | | | |
| Prothrombin fragments 1 + 2, Change at Day 33 | 685.3 (± 435.87) | | | |
| Prothrombin fragments 1 + 2, Change at Day 57 | 525.0 (± 421.78) | | | |
| Prothrombin fragments 1 + 2, Change at Day 85 | 483.9 (± 436.47) | | | |
| Prothrombin fragments 1 + 2, Change at Day 113 | -30.4 (± 135.52) | | | |

Notes:

[102] - Not all subjects were analyzed for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in D-Dimer

| | |
|-----------------|---------------------------------|
| End point title | Change From Baseline in D-Dimer |
|-----------------|---------------------------------|

End point description:

An in vivo pharmacodynamic measure of thrombin generation (fibrin degradation). D-dimer is a fibrin degradation product, a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. D-dimer is one of the protein fragments produced when a blood clot gets dissolved in the body. It is normally undetectable or detectable at a very low level unless the body is forming and breaking down blood clots. Then, its level in the blood can significantly rise.

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

End point timeframe:

Baseline, Study Day 2, 4, 8, 15, 22, 29, 30, 33, 57, 85 and 113

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[103] | 6 ^[104] | 6 ^[105] | 7 ^[106] |
| Units: microgram/milliliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| D-dimer, Change at Day 2 | 0.0393 (± 0.16303) | 0.0792 (± 0.22238) | 0.1900 (± 0.09301) | 0.1086 (± 0.30536) |
| D-dimer, Change at Day 4 | 0.2050 (± 0.24491) | 0.2842 (± 0.36896) | 0.3217 (± 0.23248) | 0.6729 (± 0.62524) |
| D-dimer, Change at Day 8 | 0.0743 (± 0.26111) | 0.2017 (± 0.29753) | 0.3292 (± 0.40635) | 0.5614 (± 0.54901) |

| | | | | |
|----------------------------|---------------------|--------------------|--------------------|---------------------|
| D-dimer, Change at Day 15 | 0.0979 (± 0.25666) | 0.1942 (± 0.28748) | 0.2500 (± 0.23424) | 0.1900 (± 0.82310) |
| D-dimer, Change at Day 22 | 0.1364 (± 0.27802) | 0.2167 (± 0.33877) | 0.2000 (± 0.26109) | 0.1829 (± 1.27802) |
| D-dimer, Change at Day 29 | 0.0633 (± 0.20029) | 0.2308 (± 0.32355) | 0.1517 (± 0.42347) | -0.0129 (± 1.17491) |
| D-dimer, Change at Day 30 | 0.1350 (± 0.32388) | 0.1492 (± 0.26345) | 0.2133 (± 0.33914) | -0.0833 (± 1.31549) |
| D-dimer, Change at Day 33 | 0.0800 (± 0.28796) | 0.1283 (± 0.37519) | 0.1233 (± 0.49855) | -0.1700 (± 1.68635) |
| D-dimer, Change at Day 57 | 0.1942 (± 0.30049) | 0.2175 (± 0.22554) | 0.1233 (± 0.36122) | 0.4033 (± 0.37120) |
| D-dimer, Change at Day 85 | 0.1664 (± 0.30521) | 0.5860 (± 1.00003) | 0.1833 (± 0.43840) | 0.2300 (± 0.60395) |
| D-dimer, Change at Day 113 | -0.1000 (± 0.22127) | 0.1875 (± 0.26517) | 0.0175 (± 0.41838) | -0.7833 (± 1.60090) |

Notes:

[103] - Not all subjects were analyzed for some specific rows of time points.

[104] - Not all subjects were analyzed for some specific rows of time points.

[105] - Not all subjects were analyzed for some specific rows of time points.

[106] - Not all subjects were analyzed for some specific rows of time points.

| | | | | |
|--------------------------------------|-------------------------------|--|--|--|
| End point values | Overall PF-06741086 300 mg SC | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 14 ^[107] | | | |
| Units: microgram/milliliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| D-dimer, Change at Day 2 | 0.0739 (± 0.23790) | | | |
| D-dimer, Change at Day 4 | 0.4389 (± 0.51676) | | | |
| D-dimer, Change at Day 8 | 0.3179 (± 0.48422) | | | |
| D-dimer, Change at Day 15 | 0.1439 (± 0.58769) | | | |
| D-dimer, Change at Day 22 | 0.1596 (± 0.88887) | | | |
| D-dimer, Change at Day 29 | 0.0223 (± 0.84172) | | | |
| D-dimer, Change at Day 30 | 0.0258 (± 0.92048) | | | |
| D-dimer, Change at Day 33 | -0.0450 (± 1.16076) | | | |
| D-dimer, Change at Day 57 | 0.2988 (± 0.34001) | | | |
| D-dimer, Change at Day 85 | 0.1958 (± 0.44682) | | | |
| D-dimer, Change at Day 113 | -0.4154 (± 1.10366) | | | |

Notes:

[107] - Not all subjects were analyzed for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dilute Prothrombin Time

| | |
|---|---|
| End point title | Change From Baseline in Dilute Prothrombin Time |
| End point description: | |
| An ex vivo pharmacodynamic measure of thrombin generation (via extrinsic pathway). Clotting time is measured using a dilute prothrombin time reagent consisting of a unique formulation of relipidated recombinant tissue factor and calcium. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Study Day 2, 4, 8, 15, 22, 29, 30, 33, 57, 85 and 113 | |

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[108] | 6 ^[109] | 6 ^[110] | 7 ^[111] |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| Dilute prothrombin Time, Change at Day 2 | -27.84 (± 21.023) | -13.32 (± 25.780) | -31.25 (± 13.606) | -17.14 (± 26.167) |
| Dilute prothrombin Time, Change at Day 4 | -30.03 (± 24.312) | -17.87 (± 20.042) | -34.50 (± 18.306) | -14.70 (± 30.971) |
| Dilute prothrombin Time, Change at Day 8 | -23.63 (± 19.991) | -15.10 (± 22.129) | -31.23 (± 19.645) | -20.97 (± 33.969) |
| Dilute prothrombin Time, Change at Day 15 | -20.73 (± 23.070) | -19.33 (± 20.853) | -33.53 (± 14.880) | 1.11 (± 27.208) |
| Dilute prothrombin Time, Change at Day 22 | -21.40 (± 22.351) | -10.55 (± 16.057) | -26.78 (± 32.501) | -21.61 (± 30.842) |
| Dilute prothrombin Time, Change at Day 29 | -15.32 (± 13.867) | -7.10 (± 20.643) | -40.40 (± 22.458) | -18.03 (± 24.600) |
| Dilute prothrombin Time, Change at Day 30 | -13.27 (± 13.399) | -23.45 (± 19.413) | -45.18 (± 21.372) | -17.47 (± 25.729) |
| Dilute prothrombin Time, Change at Day 33 | -23.35 (± 17.690) | -21.23 (± 20.010) | -29.10 (± 20.783) | -19.97 (± 19.297) |
| Dilute prothrombin Time, Change at Day 57 | -14.75 (± 14.393) | -12.03 (± 30.806) | -26.80 (± 12.911) | -11.72 (± 42.872) |
| Dilute prothrombin Time, Change at Day 85 | -20.99 (± 25.424) | -25.80 (± 24.334) | -23.43 (± 26.166) | -12.42 (± 34.871) |
| Dilute prothrombin Time, Change at Day 113 | -16.44 (± 13.578) | 14.30 (± 61.235) | -39.63 (± 20.182) | -12.78 (± 28.226) |

Notes:

[108] - Not all subjects were analyzed for some specific rows of time points.

[109] - Not all subjects were analyzed for some specific rows of time points.

[110] - Not all subjects were analyzed for some specific rows of time points.

[111] - Not all subjects were analyzed for some specific rows of time points.

| End point values | Overall PF-06741086 300 mg SC | | | |
|--------------------------------------|-------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 14 ^[112] | | | |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | | | | |

| | | | | |
|--|-------------------|--|--|--|
| Dilute prothrombin Time, Change at Day 2 | -22.49 (± 23.470) | | | |
| Dilute prothrombin Time, Change at Day 4 | -22.36 (± 27.907) | | | |
| Dilute prothrombin Time, Change at Day 8 | -22.30 (± 26.813) | | | |
| Dilute prothrombin Time, Change at Day 15 | -9.81 (± 26.753) | | | |
| Dilute prothrombin Time, Change at Day 22 | -21.51 (± 25.877) | | | |
| Dilute prothrombin Time, Change at Day 29 | -16.78 (± 19.613) | | | |
| Dilute prothrombin Time, Change at Day 30 | -15.37 (± 19.680) | | | |
| Dilute prothrombin Time, Change at Day 33 | -21.66 (± 17.737) | | | |
| Dilute prothrombin Time, Change at Day 57 | -13.23 (± 30.531) | | | |
| Dilute prothrombin Time, Change at Day 85 | -17.03 (± 29.148) | | | |
| Dilute prothrombin Time, Change at Day 113 | -14.75 (± 20.682) | | | |

Notes:

[112] - Not all subjects were analyzed for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Tested Positive for Anti-PF-06741086 Antibody (ADA)

| | |
|--|--|
| End point title | Number of Subjects Who Tested Positive for Anti-PF-06741086 Antibody (ADA) |
| End point description: Human plasma ADA samples were analyzed for the detection of anti PF-06741086 antibodies by using semi-quantitative electrochemiluminescence (ECL) method. The criterion for positive result of ADA samples was ADA titer ≥ 1.53 . Treatment induced are negative prior to dosing and become positive during/after dosing. Treatment boosted are positive prior to dosing but titer increases during/after dosing. | |
| End point type | Secondary |
| End point timeframe: Baseline up to Study Day 113 | |

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 6 | 7 |
| Units: Subjects | | | | |
| ADA incidence | 0 | 1 | 2 | 0 |
| Subjects with treatment induced ADA incidence | 0 | 1 | 2 | 0 |

| | | | | |
|---|---|---|---|---|
| Subjects with treatment boosted ADA incidence | 0 | 0 | 0 | 0 |
|---|---|---|---|---|

| End point values | Overall PF-06741086 300 mg SC | Total | | |
|---|-------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 14 | 26 | | |
| Units: Subjects | | | | |
| ADA incidence | 0 | 3 | | |
| Subjects with treatment induced ADA incidence | 0 | 3 | | |
| Subjects with treatment boosted ADA incidence | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Tested Positive for Neutralizing Antibody (NAb)

| | |
|-----------------|--|
| End point title | Number of Subjects Who Tested Positive for Neutralizing Antibody (NAb) |
|-----------------|--|

End point description:

Human plasma NAb samples were analyzed for the presence or absence of NAb to PF 06741086 using semi-quantitative electrochemiluminescence (ECL) method. Treatment induced are negative prior to dosing and become positive during/after dosing. Treatment boosted are positive prior to dosing but titer increases during/after dosing.

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

End point timeframe:

Baseline up to Study Day 113

| End point values | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC QW Inhibitor |
|---|--|--|--|------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[113] | 1 | 2 | 0 ^[114] |
| Units: Subjects | | | | |
| NAb incidence | | 0 | 0 | |
| Subjects with treatment induced NAb incidence | | 0 | 0 | |
| Subjects with treatment boosted NAb incidence | | 0 | 0 | |

Notes:

[113] - Only subjects who had positive ADA sample were tested in the NAb assay.

[114] - Only subjects who had positive ADA sample were tested in the NAb assay.

| End point values | Overall PF-06741086 300 mg SC | Total | | |
|---|-------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 0 ^[115] | 3 | | |
| Units: Subjects | | | | |
| NAb incidence | | 0 | | |
| Subjects with treatment induced NAb incidence | | 0 | | |
| Subjects with treatment boosted NAb incidence | | 0 | | |

Notes:

[115] - Only subjects who had positive ADA sample were tested in the NAb assay.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

113 days

Adverse event reporting additional description:

The same event may appear as both an AE and an SAE. 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. Total number at risk below refers to the number of subjects evaluable for SAEs or AEs.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 21.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | PF-06741086 300 mg SC QW Non-Inhibitor |
|-----------------------|--|

Reporting group description:

Subjects without inhibitors to FVIII or FIX in this cohort received PF-06741086 300 mg subcutaneously (SC) once weekly (QW) from Day 1 to Day 78.

| | |
|-----------------------|--|
| Reporting group title | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor |
|-----------------------|--|

Reporting group description:

Subjects without inhibitors to FVIII or FIX in this cohort received PF-06741086 300 mg loading dose on Day 1 and 150 mg SC QW from Day 8 to Day 78.

| | |
|-----------------------|--|
| Reporting group title | PF-06741086 450 mg SC QW Non-Inhibitor |
|-----------------------|--|

Reporting group description:

Subjects without inhibitors to FVIII or FIX in this cohort received PF-06741086 450 mg SC QW from Day 1 to Day 78.

| | |
|-----------------------|------------------------------------|
| Reporting group title | PF-06741086 300 mg SC QW Inhibitor |
|-----------------------|------------------------------------|

Reporting group description:

Subjects with inhibitors to FVIII or FIX in this cohort received PF-06741086 300 mg SC QW from Day 1 to Day 78.

| | |
|-----------------------|-------------------------------|
| Reporting group title | Overall PF-06741086 300 mg SC |
|-----------------------|-------------------------------|

Reporting group description:

The overall PF-06741086 300 mg SC group combined subjects from both the PF-06741086 300 mg SC QW non-inhibitor and inhibitor dose cohorts.

| | |
|-----------------------|-------|
| Reporting group title | Total |
|-----------------------|-------|

Reporting group description:

The total group combined subjects from all PF-06741086 cohorts in this study.

| Serious adverse events | PF-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 6 (16.67%) | 1 / 6 (16.67%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Social circumstances | | | |

| | | | |
|---|----------------|----------------|----------------|
| Physical assault | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (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 |
| Gastrointestinal disorders | | | |
| Tooth socket haemorrhage | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (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 |

| Serious adverse events | PF-06741086 300 mg SC QW Inhibitor | Overall PF-06741086 300 mg SC | Total |
|---|------------------------------------|-------------------------------|-----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 14 (14.29%) | 4 / 26 (15.38%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Social circumstances | | | |
| Physical assault | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 14 (0.00%) | 1 / 26 (3.85%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Tooth socket haemorrhage | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 14 (7.14%) | 1 / 26 (3.85%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |

| | | | |
|---|---------------|----------------|----------------|
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 14 (0.00%) | 1 / 26 (3.85%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 14 (7.14%) | 1 / 26 (3.85%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| 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-06741086 300 mg SC QW Non-Inhibitor | PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor | PF-06741086 450 mg SC QW Non-Inhibitor |
|---|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 6 / 7 (85.71%) | 4 / 6 (66.67%) | 6 / 6 (100.00%) |
| Investigations | | | |
| Blood fibrinogen decreased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fibrin D dimer increased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Prothrombin time prolonged | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Troponin I increased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Troponin increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Occupational exposure to product subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Road traffic accident subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 2 / 6 (33.33%) 2 | 1 / 6 (16.67%) 1 |
| Nervous system disorders Cerebrospinal fluid leakage subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Dizziness subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 2 / 6 (33.33%) 2 |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Injection site bruising subjects affected / exposed occurrences (all) | 2 / 7 (28.57%) 2 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Injection site erythema subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Injection site haemorrhage subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Injection site induration | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Injection site pain | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 6 (16.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 1 | 6 |
| Injection site pruritus | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site swelling | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 0 | 3 |
| Injection site warmth | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastroesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus generalised | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash erythematous | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|-----------------------------------|----------------|----------------|----------------|
| Arthralgia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Haemarthrosis | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Haemophilic arthropathy | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Infections and infestations | | | |
| Influenza | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Periodontitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| Non-serious adverse events | PF-06741086 300 mg SC QW Inhibitor | Overall PF-06741086 300 mg SC | Total |
|---|------------------------------------|-------------------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 7 (57.14%) | 10 / 14 (71.43%) | 20 / 26 (76.92%) |
| Investigations | | | |
| Blood fibrinogen decreased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 14 (7.14%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 | 1 |
| Fibrin D dimer increased | | | |

| | | | |
|--|---------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 14 (7.14%) 1 | 1 / 26 (3.85%) 1 |
| Prothrombin time prolonged subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 1 / 14 (7.14%) 1 | 2 / 26 (7.69%) 2 |
| Troponin I increased subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 2 / 14 (14.29%) 2 | 2 / 26 (7.69%) 2 |
| Troponin increased subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 26 (3.85%) 1 |
| Injury, poisoning and procedural complications | | | |
| Contusion subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 14 (7.14%) 1 | 2 / 26 (7.69%) 2 |
| Occupational exposure to product subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 14 (7.14%) 1 | 1 / 26 (3.85%) 1 |
| Road traffic accident subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 26 (3.85%) 1 |
| Vascular disorders | | | |
| Hypertension subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 14 (0.00%) 0 | 3 / 26 (11.54%) 3 |
| Nervous system disorders | | | |
| Cerebrospinal fluid leakage subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 14 (7.14%) 1 | 1 / 26 (3.85%) 1 |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 14 (7.14%) 1 | 1 / 26 (3.85%) 1 |
| Headache subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 14 (0.00%) 0 | 2 / 26 (7.69%) 2 |
| General disorders and administration site conditions | | | |

| | | | |
|----------------------------------|----------------|-----------------|-----------------|
| Fatigue | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 14 (7.14%) | 2 / 26 (7.69%) |
| occurrences (all) | 0 | 1 | 2 |
| Injection site bruising | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 14 (14.29%) | 2 / 26 (7.69%) |
| occurrences (all) | 0 | 2 | 2 |
| Injection site erythema | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 14 (7.14%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 | 1 |
| Injection site haemorrhage | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 14 (7.14%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 | 1 |
| Injection site induration | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 14 (7.14%) | 2 / 26 (7.69%) |
| occurrences (all) | 0 | 1 | 2 |
| Injection site pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 14 (7.14%) | 3 / 26 (11.54%) |
| occurrences (all) | 0 | 2 | 9 |
| Injection site pruritus | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 14 (7.14%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 | 1 |
| Injection site swelling | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 14 (7.14%) | 3 / 26 (11.54%) |
| occurrences (all) | 1 | 1 | 4 |
| Injection site warmth | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 14 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 14 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 2 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 14 (7.14%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 1 | 1 |
| Gastrooesophageal reflux disease | | | |

| | | | |
|--|---|--|--|
| subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 26 (3.85%) 1 |
| Respiratory, thoracic and mediastinal disorders Rhinitis allergic subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 26 (3.85%) 1 |
| Skin and subcutaneous tissue disorders Pruritus generalised subjects affected / exposed occurrences (all) Rash erythematous subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1 | 1 / 14 (7.14%) 1 1 / 14 (7.14%) 1 | 1 / 26 (3.85%) 1 1 / 26 (3.85%) 1 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Bursitis subjects affected / exposed occurrences (all) Haemarthrosis subjects affected / exposed occurrences (all) Haemophilic arthropathy subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 0 / 7 (0.00%) 0 0 / 7 (0.00%) 0 0 / 7 (0.00%) 0 0 / 7 (0.00%) 0 | 2 / 14 (14.29%) 3 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0 1 / 14 (7.14%) 1 0 / 14 (0.00%) 0 | 2 / 26 (7.69%) 3 1 / 26 (3.85%) 1 1 / 26 (3.85%) 1 1 / 26 (3.85%) 1 |
| Infections and infestations Influenza subjects affected / exposed occurrences (all) Periodontitis subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1 | 1 / 14 (7.14%) 1 1 / 14 (7.14%) 1 | 2 / 26 (7.69%) 2 2 / 26 (7.69%) 2 |

| | | | |
|---|--------------------|---------------------|---------------------|
| Respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 26 (3.85%) 1 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 14 (7.14%) 1 | 1 / 26 (3.85%) 1 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 09 September 2016 | 1. Added EudraCT # on protocol title page 2.Revised inclusion criterion #2 to restrict subjects from ≥ 12 and < 18 years of age to cohorts at a dose level and route of administration previously studied which has not met the protocol safety criteria for termination of dose escalation. |
| 02 November 2016 | 1. Added US IND # to protocol 2. Revised nominal doses planned for Cohorts 2 through 4 added to new section (1.3.3.2 Dose Progression). 3.Removed option for self administration for SC cohorts and specified visits for SC cohorts. 4.Inclusion Criterion #5: criterion was revised to state that only patients currently treated with episodic (on demand) factor replacement therapy are eligible for this study. |
| 12 December 2016 | 1.Added new criteria and references for dose escalation and stopping rules. 2.Revised Inclusion Criterion #2 to state that only adult subjects (18 to 65 years of age) are eligible for the study, added Exclusion Criterion #4 to state that subjects with pro thrombotic conditions are excluded from the study. |
| 02 October 2017 | 1.Removed "AND" from "AND/OR" to conform to previous amendment that removed a combination subcutaneous and intravenous dose. 2. Added language anywhere applicable allowing for the inclusion of subjects with inhibitors against FVIII or FIX and specified analyses for inhibitor subjects. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported