Clinical trial results:
A Phase 2, 24-Week, Adaptive, Open Label, Sequential Cohort Trial To Evaluate The Efficacy, Safety, Tolerability and Pharmacokinetics of PF-06730512 Following Multiple Doses in Adult Subjects With Focal Segmental Glomerulosclerosis (FSGS)

Summary

EudraCT number	2019-003607-35
Trial protocol	DE SK PL CZ IT
Global end of trial date	14 February 2023

Results information

Result version number	v1 (current)
This version publication date	17 February 2024
First version publication date	17 February 2024

Trial information

Trial identification

Sponsor protocol code	C0221002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03448692
WHO universal trial number (UTN)	-
Other trial identifiers	ROBO2/PODO: C0221002

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 Centre, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Centre, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 September 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 February 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of PF-06730512 compared to baseline in the reduction of proteinuria following 12 weeks of treatment in subjects with FSGS.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 October 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Czechia: 2
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Japan: 5
Country: Number of subjects enrolled	Mexico: 1
Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	Slovakia: 5
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	United States: 18
Worldwide total number of subjects	47
EEA total number of subjects	17

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	45
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 47 subjects were enrolled into the study. All subjects received treatment.

Period 1

Period 1 title	Disposition Phase:Screening:up to 43Days
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	PF-06730512 1000 mg IV

Arm description:

Subjects received PF-06730512 1000 milligram (mg) intravenously (IV) every 2 weeks (Q2W).

Arm type	Experimental
Investigational medicinal product name	PF-06730512
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received PF-06730512 1000 mg IV Q2W.

Arm title	PF-06730512 300 mg IV

Arm description:

Subjects received PF-06730512 300 mg IV Q2W.

Arm type	Experimental
Investigational medicinal product name	PF-06730512
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received PF-06730512 300 mg IV Q2W.

Number of subjects in period 1	PF-06730512 1000 mg IV	PF-06730512 300 mg IV
Started	23	24
Completed	23	24

Period 2

Period 2 title	Lead in Period:8 Weeks (W)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	PF-06730512 1000 mg IV

Arm description:

Subjects received PF-06730512 1000 milligram (mg) intravenously (IV) every 2 weeks (Q2W).

Arm type	Experimental
Investigational medicinal product name	PF-06730512
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received PF-06730512 1000 mg IV Q2W.

Arm title	PF-06730512 300 mg IV

Arm description:

Subjects received PF-06730512 300 mg IV Q2W.

Arm type	Experimental
Investigational medicinal product name	PF-06730512
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received PF-06730512 300 mg IV Q2W.

Number of subjects in period 2	PF-06730512 1000 mg IV	PF-06730512 300 mg IV
Started	23	24
Completed	23	24

Period 3

Period 3 title	Investigational Treatment Period:Upto24W
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	PF-06730512 1000 mg IV

Arm description:

Subjects received PF-06730512 1000 milligram (mg) intravenously (IV) every 2 weeks (Q2W).

Arm type	Experimental
Investigational medicinal product name	PF-06730512
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received PF-06730512 1000 mg IV Q2W.

Arm title	PF-06730512 300 mg IV

Arm description:

Subjects received PF-06730512 300 mg IV Q2W.

Arm type	Experimental
Investigational medicinal product name	PF-06730512
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received PF-06730512 300 mg IV Q2W.

Number of subjects in period 3	PF-06730512 1000 mg IV	PF-06730512 300 mg IV
Started	23	24
Completed	22	15
Not completed	1	9
Consent withdrawn by subject	-	2
Adverse event, non-fatal	1	-
Study terminated by sponsor	-	5
Lack of efficacy	-	1
Physician's decision	-	1

Period 4

Period 4 title	Follow up Period: 9 Weeks
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	PF-06730512 1000 mg IV

Arm description:

Subjects received PF-06730512 1000 milligram (mg) intravenously (IV) every 2 weeks (Q2W).

Arm type	Experimental
Investigational medicinal product name	PF-06730512
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received PF-06730512 1000 mg IV Q2W.

Arm title	PF-06730512 300 mg IV

Arm description:

Subjects received PF-06730512 300 mg IV Q2W.

Arm type	Experimental
Investigational medicinal product name	PF-06730512
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received PF-06730512 300 mg IV Q2W.

Number of subjects in period 4	PF-06730512 1000 mg IV	PF-06730512 300 mg IV
Started	22	15
Completed	23	23

Joined	1	8
Continued follow-up	1	8

Baseline characteristics

Reporting groups

Reporting group title	Disposition Phase:Screening:up to 43Days

Reporting group description: -

Reporting group values	Disposition Phase:Screening:up to 43Days	Total	
Number of subjects	47	47	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	45	45	
From 65-84 years	2	2	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	41.8		
standard deviation	± 14.01	-	
Sex: Female, Male Units: Subjects			
Female	22	22	
Male	25	25	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	8	8	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	2	2	
White	36	36	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	8	8	
Not Hispanic or Latino	39	39	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	PF-06730512 1000 mg IV
Reporting group description: Subjects received PF-06730512 1000 milligram (mg) intravenously (IV) every 2 weeks (Q2W).	
Reporting group title	PF-06730512 300 mg IV
Reporting group description: Subjects received PF-06730512 300 mg IV Q2W.	
Reporting group title	PF-06730512 1000 mg IV
Reporting group description: Subjects received PF-06730512 1000 milligram (mg) intravenously (IV) every 2 weeks (Q2W).	
Reporting group title	PF-06730512 300 mg IV
Reporting group description: Subjects received PF-06730512 300 mg IV Q2W.	
Reporting group title	PF-06730512 1000 mg IV
Reporting group description: Subjects received PF-06730512 1000 milligram (mg) intravenously (IV) every 2 weeks (Q2W).	
Reporting group title	PF-06730512 300 mg IV
Reporting group description: Subjects received PF-06730512 300 mg IV Q2W.	
Reporting group title	PF-06730512 1000 mg IV
Reporting group description: Subjects received PF-06730512 1000 milligram (mg) intravenously (IV) every 2 weeks (Q2W).	
Reporting group title	PF-06730512 300 mg IV
Reporting group description: Subjects received PF-06730512 300 mg IV Q2W.	

Primary: Percentage Change From Baseline in Urinary Protein to Creatinine Ratio (UPCR) Based on 24-hour Urine Collection at Week 13

End point title	Percentage Change From Baseline in Urinary Protein to Creatinine Ratio (UPCR) Based on 24-hour Urine Collection at Week 13[1]

End point description:

UPCR is a ratio between two measured substances in urine: milligram of protein per millimole (mmol) of creatinine, reported in units mg/mmol. A decrease in UPCR may be associated with improved renal and cardiovascular function. The Full Analysis Set (FAS) was defined as all enrolled subjects who had received at least one dose of study treatment and had at least one post-baseline measurement of UPCR based on 24-hour urine collection. Here, "Number of Subjects Analysed" signifies subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Week 13

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: Only descriptive analysis was planned for this endpoint.

End point values	PF-06730512 1000 mg IV	PF-06730512 300 mg IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	19		
Units: Percentage change				
least squares mean (confidence interval 90%)	-12.283 (-26.096 to 4.112)	-0.045 (-9.528 to 10.432)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormalities in Laboratory Test Parameters

End point title	Number of Subjects With Abnormalities in Laboratory Test Parameters

End point description:

Hemoglobin(Hg),hematocrit,erythrocytes:<0.8*lower limits of normal(LLN);platelets:<0.5*LLN>1.75*upper LN leukocytes(leu),glucose-fasting:<0.6*LLN>1.5*ULN;lymphocytes(lym),lym/leu, neutrophils(neu),neu/leu,protein,albumin,phosphate,free thyroxine,thyroid stimulating hormone: <0.8*LLN>1.2*ULN;basophils(bas),bas/leu,eosinophils(eos),eos/leu,monocytes(mon),mon/leu:>1.2*ULN;bilirubin (total, direct, indirect):>1.5*ULN;aspartate aminotransferase(AT),alanine AT,lactate dehydrogenase,alkaline phosphatase:>3.0*ULN;blood urea nitrogen,creatinine,cholesterol(total,LDL,HDL),triglycerides,Hg A1C: >1.3*ULN;sodium:<0.95*LLN>1.05*ULN;potassium,chloride,calcium,magnesium,bicarbonate:<0.9*LLN >1.1*ULN;prolactin:>1.1*ULN;creatine kinase:>2.0*ULN;urobilinogen:>=1;Urine-specific gravity:<1.003>1.030,pH:<4.5 >8, glucose,protein,bilirubin,nitrite,leukocyte esterase,

End point type	Secondary

End point timeframe:

From Day 1 of treatment up to Week 33

End point values	PF-06730512 1000 mg IV	PF-06730512 300 mg IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	24		
Units: Subjects				
Hg<0.8*LLN (n=23,24)	5	4		
Hematocrit<0.8*LLN (n=23,24)	5	7		
Erythrocytes<0.8*LLN (n=23,24)	3	4		
Ery. Mean Corpuscular Volume < 0.9*LLN (n=23,24)	1	0		
Ery. Mean Corpuscular Hg<0.9*LLN (n=23,24)	1	0		
Platelets>1.75*ULN (n=23,24)	1	0		
Lym<0.8*LLN (n=23,24)	0	4		
Lym/Leu<0.8*LLN (n=23,24)	1	6		
Lym/Leu>1.2*ULN (n=23,24)	0	1		
Neu <0.8*LLN (n=23,24)	1	2		
Neu >1.2*ULN (n=23,24)	3	4		
Neu/Leu<0.8*LLN (n=23,24)	1	1		

Neu/Leu>1.2*ULN (n=23,24)	0	1		
Eos>1.2*ULN (n=23,24)	2	1		
Eos/Leu>1.2*ULN (n=23,24)	3	3		
Mon/Leu>1.2*ULN (n=23,24)	0	1		
Aspartate AT>3.0*ULN (n=23,23)	1	0		
Alanine AT>3.0*ULN (n=23,23)	1	0		
Protein<0.8*LLN (n=23,23)	9	11		
Albumin<0.8*LLN (n=23,23)	8	11		
Blood Urea Nitrogen>1.3*ULN (n=23,23)	10	8		
Creatinine>1.3*ULN (n=23,23)	8	12		
Urate>1.2*ULN (n=23,23)	3	2		
Cholesterol >1.3*ULN (n=23,23)	6	7		
HDL Cholesterol<0.8 *LLN (n=23,2)	1	0		
LDL Cholesterol>1.2*ULN (n=23,22)	6	5		
Triglycerides>1.3*ULN (n=23,23)	6	8		
Sodium<0.95*LLN (n=23,23)	1	0		
Potassium<0.9*LLN (n=23,23)	1	0		
Potassium>1.1*ULN (n=23,23)	1	0		
Calcium<0.9*LLN (n=23,23)	1	3		
Bicarbonate<0.9*LLN (n=23,23)	0	1		
Glucose>1.5*ULN (n=23,23)	2	2		
Specific Gravity>1.030 (n=21,24)	5	6		
pH>8 (n=23,24)	1	0		
Urine Glucose>=1 (n=23,24)	5	10		
Urine Protein>=1 (n=23,24)	22	24		
Urine Hemoglobin>=1 (n=23,24)	15	17		
Nitrite>=1 (n=23,24)	1	3		
Leukocyte Esterase>=1 (n=23,24)	5	6		
Urine Erythrocytes>=20 (n=22,24)	3	3		
Urine Leukocytes>=20 (n=22,24)	2	5		
Granular Casts>1 (n=5,2)	4	2		
Hyaline Casts>1 (n=18,18)	17	15		
Urine Creatinine<40(n=23,24)	9	8		
Urine Creatinine>300 (n=23,24)	1	0		
Urine (24HR) Creatinine>1.1*ULN (n=23,24)	2	6		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point description:

An adverse event was considered treatment emergent relative to a given treatment if the event occurred for the first time during the investigational treatment period and was not seen prior to the start of treatment (during the lead-in period), or the event was seen prior to the start of treatment but increased in severity during treatment. Adverse events occurring during the lead-in period were considered non-treatment emergent. Events that occurred during the follow-up period were counted as

treatment emergent and attributed to the previous treatment taken. SAS was defined as all enrolled subjects who had received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

From Day 1 of treatment up to 9 weeks after last dose of study treatment (up to Week 33)

End point values	PF-06730512 1000 mg IV	PF-06730512 300 mg IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	24		
Units: Subjects	20	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Weight

End point title	Change From Baseline in Body Weight

End point description:

Change from baseline in body weight and at baseline values were reported for this endpoint. SAS was defined as all enrolled subjects who had received at least one dose of study treatment. Here, 'Number Analysed' (n) signifies number of subjects evaluable for the specific timepoints.

End point type	Secondary

End point timeframe:

Baseline, Change at Weeks 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 33

End point values	PF-06730512 1000 mg IV	PF-06730512 300 mg IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	24		
Units: Kilogram				
arithmetic mean (standard deviation)				
Baseline (n=23,24)	78.3 (± 17.8)	88.9 (± 23.5)		
Week 2 (n=23,24)	1.0 (± 2.2)	-0.3 (± 1.9)		
Week 3 (n=23,23)	0.4 (± 2.5)	-0.3 (± 2.2)		
Week 5 (n=22,23)	0.5 (± 3.0)	-0.5 (± 4.8)		
Week 7 (n=23,22)	0.6 (± 2.6)	-1.0 (± 5.3)		
Week 9 (n=22,22)	0.1 (± 3.1)	-0.4 (± 3.4)		
Week 11 (n=22,20)	0.7 (± 2.8)	-0.1 (± 4.2)		
Week 13 (n=23,22)	-0.2 (± 1.9)	-1.0 (± 3.4)		
Week15 (n=4,13)	-0.3 (± 1.0)	-0.7 (± 4.0)		
Week 17 (n=4,9)	-0.2 (± 1.2)	-1.2 (± 4.8)		
Week 19 (n=4,9)	-0.4 (± 1.0)	-1.3 (± 4.8)		
Week 21 (n=4,9)	0.3 (± 1.7)	-1.3 (± 4.9)		
Week 23 (n=4,9)	0.3 (± 1.2)	-1.5 (± 5.3)		

Week 25 (n=4,16)	-0.1 (± 1.6)	-1.1 (± 4.8)		
Week 27 (n=4,16)	0.7 (± 1.4)	-0.6 (± 5.2)		
Week 29 (n=4,16)	0.5 (± 1.5)	-1.0 (± 4.5)		
Week 33 (n=4,16)	0.5 (± 1.6)	-0.6 (± 5.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Blood Pressure

End point title	Change From Baseline in Blood Pressure

End point description:

Change from baseline in blood pressure and at baseline values were reported for this endpoint. SAS was defined as all enrolled subjects who had received at least one dose of study treatment. Here, 'Number Analysed' signifies number of subjects evaluable for the specific timepoints.

End point type	Secondary

End point timeframe:

Baseline, Change at Weeks 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 33

End point values	PF-06730512 1000 mg IV	PF-06730512 300 mg IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	24		
Units: Millimetre of mercury (mmHg)				
arithmetic mean (standard deviation)				
Baseline (n=23,24)	131.2 (± 12.8)	125.3 (± 11.8)		
Week 2 (n=23,24)	-1.8 (± 13.1)	-1.3 (± 7.8)		
Week 3 (n=23,23)	-1.3 (± 10.2)	1.7 (± 7.5)		
Week 5 (n=22,23)	-3.0 (± 10.6)	-1.9 (± 9.0)		
Week 7 (n=23,22)	-2.0 (± 11.3)	-1.2 (± 9.0)		
Week 9 (n=22,22)	-5.1 (± 10.7)	-2.6 (± 7.6)		
Week 11 (n=22,20)	-1.5 (± 12.5)	-1.6 (± 6.1)		
Week 13 (n=23,22)	-2.0 (± 11.3)	-1.0 (± 10.0)		
Week15 (n=4,13)	-7.5 (± 5.1)	-2.3 (± 6.2)		
Week 17 (n=4,9)	-7.3 (± 12.7)	-7.7 (± 12.2)		
Week 19 (n=4,9)	-8.0 (± 8.4)	0.4 (± 10.7)		
Week 21 (n=4,9)	-8.0 (± 16.4)	-5.8 (± 10.1)		
Week 23 (n=4,9)	1.0 (± 9.0)	-3.6 (± 8.2)		
Week 25 (n=4,16)	-9.0 (± 13.2)	-2.6 (± 11.2)		
Week 27 (n=4,16)	-3.0 (± 10.4)	3.5 (± 10.5)		
Week 29 (n=4,16)	-8.3 (± 8.4)	0.4 (± 11.2)		
Week 33 (n=4,16)	-12.0 (± 20.7)	4.6 (± 8.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pulse Rate

End point title	Change From Baseline in Pulse Rate

End point description:

Change from baseline in pulse rate and at baseline values were reported for this endpoint. SAS was defined as all enrolled subjects who had received at least one dose of study treatment. Here, 'Number Analysed' signifies number of subjects evaluable for the specific timepoints.

End point type	Secondary

End point timeframe:

Baseline, Change at Weeks 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 33

End point values	PF-06730512 1000 mg IV	PF-06730512 300 mg IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	24		
Units: Beats per minute				
arithmetic mean (standard deviation)				
Baseline (n=23,24)	74.1 (± 11.8)	74.2 (± 11.0)		
Week 2 (n=23,24)	2.1 (± 9.6)	0.6 (± 6.9)		
Week 3 (n=23,23)	-0.6 (± 8.0)	-1.1 (± 6.0)		
Week 5 (n=22,23)	0.0 (± 7.3)	-0.3 (± 8.0)		
Week 7 (n=23,22)	-0.3 (± 9.2)	0.0 (± 7.9)		
Week 9 (n=22,22)	-1.0 (± 11.1)	1.5 (± 9.0)		
Week 11 (n=22,20)	-1.7 (± 10.8)	0.6 (± 6.6)		
Week 13 (n=23,22)	3.3 (± 11.9)	0.5 (± 6.9)		
Week 15 (n=4,13)	-5.8 (± 10.4)	5.0 (± 10.1)		
Week 17 (n=4,9)	-6.3 (± 8.8)	-2.2 (± 5.0)		
Week 19 (n=4,9)	-3.5 (± 13.7)	2.9 (± 6.5)		
Week 21 (n=4,9)	-5.5 (± 12.8)	-1.6 (± 5.0)		
Week 23 (n=4,9)	-3.3 (± 10.5)	-3.1 (± 9.0)		
Week 25 (n=4,16)	-6.3 (± 12.5)	1.8 (± 7.6)		
Week 27 (n=4,16)	-0.8 (± 16.0)	2.9 (± 7.2)		
Week 29 (n=4,16)	2.5 (± 14.8)	5.9 (± 8.8)		
Week 33 (n=4,16)	-0.5 (± 15.3)	6.2 (± 10.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Temperature

End point title	Change From Baseline in Body Temperature

End point description:

Change from baseline in body temperature and at baseline values were reported for this endpoint. SAS was defined as all enrolled subjects who had received at least one dose of study treatment. Here, 'Number Analysed' signifies number of subjects evaluable for the specific timepoints.

End point type	Secondary

End point timeframe:

Baseline, Change at Weeks 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 33

End point values	PF-06730512 1000 mg IV	PF-06730512 300 mg IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	24		
Units: Degree Celsius				
arithmetic mean (standard deviation)				
Baseline (n=23,24)	36.4 (± 0.4)	36.6 (± 0.2)		
Week 2 (n=23,24)	0.1 (± 0.4)	-0.0 (± 0.3)		
Week 3 (n=23,23)	0.0 (± 0.2)	-0.1 (± 0.3)		
Week 5 (n=22,23)	0.0 (± 0.4)	-0.1 (± 0.3)		
Week 7 (n=23,22)	0.1 (± 0.3)	-0.0 (± 0.3)		
Week 9 (n=22,22)	0.0 (± 0.4)	-0.1 (± 0.3)		
Week 11 (n=22,20)	0.1 (± 0.3)	-0.0 (± 0.3)		
Week 13 (n=23,22)	-0.1 (± 0.4)	-0.0 (± 0.2)		
Week 15 (n=4,13)	0.2 (± 0.2)	0.1 (± 0.2)		
Week 17 (n=4,9)	0.1 (± 0.2)	0.1 (± 0.2)		
Week 19 (n=4,9)	0.1 (± 0.4)	0.1 (± 0.3)		
Week 21 (n=4,9)	-0.0 (± 0.1)	-0.1 (± 0.5)		
Week 23 (n=4,9)	0.2 (± 0.2)	0.0 (± 0.3)		
Week 25 (n=4,16)	0.1 (± 0.2)	0.0 (± 0.2)		
Week 27 (n=4,16)	0.1 (± 0.1)	0.1 (± 0.2)		
Week 29 (n=4,16)	0.1 (± 0.3)	-0.1 (± 0.4)		
Week 33 (n=4,16)	0.1 (± 0.1)	-0.1 (± 0.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormalities in Electrocardiogram (ECG)

End point title	Number of Subjects With Abnormalities in Electrocardiogram (ECG)

End point description:

ECG abnormalities criteria included: 1) QTc interval adjusted according to Bazett formula (QTcB) in millisecond (msec): greater than (>) 450, >480, >500, increase from baseline >30, increase from baseline >60; 2) QTc interval adjusted according to Fridericia formula (QTcF) (msec): >450, >480, >500, increase from baseline >30, increase from baseline >60; 3) Heart rate (bpm): RR decrease >25% and to a VR (interval between QRS wave and T wave on ECG) >100; RR (interval between 2 successive R waves on ECG) increase >25% and to a VR <50; 4) Pulse rate (msec): increase >25% and to a value >200; 5) QT (msec): >450, >480, >500, increase from baseline >30, increase from baseline >60; 6) QRS (msec): increase >25% and to a value >110. Categories (timepoints) with at least 1 subject having ECG abnormality in any of the reporting arms, were reported for this endpoint. SAS population was analyzed. N= subjects evaluable for this endpoint. n= subjects evaluable for specific timepoints.

End point type	Secondary

End point timeframe:

Weeks 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 33

End point values	PF-06730512 1000 mg IV	PF-06730512 300 mg IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	23		
Units: Subjects				
Week 3 (Not Clinically Significant) (n=23,23)	3	4		
Week 3 (Clinically Significant) (n=23,23)	1	0		
Week 7 (Not Clinically Significant) (n=22,22)	3	4		
Week 7 (Clinically Significant) (n=22,22)	0	0		
Week 11 (Not Clinically Significant) (n=22,20)	4	4		
Week 11 (Clinically Significant) (n=22,20)	1	0		
Week 13 (Not Clinically Significant) (n=23,22)	6	4		
Week 13 (Clinically Significant) (n=23,22)	1	0		
Week 17 (Not Clinically Significant) (n=4,9)	0	0		
Week 17 (Clinically Significant) (n=4,9)	0	0		
Week 21 (Not Clinically Significant) (n=4,9)	1	1		
Week 21 (Clinically Significant) (n=4,9)	0	0		
Week 25 (Not Clinically Significant) (n=4,16)	1	1		
Week 25 (Clinically Significant) (n=4,16)	0	0		
Week 33 (Not Clinically Significant) (n=3,16)	0	2		
Week 33 (Clinically Significant) (n=3,16)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Baseline in Urinary Protein to Creatinine Ratio (UPCR) at Weeks 2, 5, 9 and 13

End point title	Percentage Change From Baseline in Urinary Protein to Creatinine Ratio (UPCR) at Weeks 2, 5, 9 and 13

End point description:

UPCR is a ratio between two measured substances in urine: mmol of creatinine, reported in units mg/mmol. A decrease in UPCR may be associated with improved renal and cardiovascular function. FAS was defined as all enrolled subjects who had received at least one dose of study treatment and had at least one post-baseline measurement of UPCR based on 24-hour urine collected. Here, 'Number Analysed' signifies number of subjects evaluable for the specific timepoints.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 5, 9 and 13

End point values	PF-06730512 1000 mg IV	PF-06730512 300 mg IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	24		
Units: Percent change				
least squares mean (confidence interval 90%)				
Week 2 (n=0,0)	0 (0 to 0)	0 (0 to 0)		
Week 5 (n=20,20)	6.250 (-7.035 to 21.433)	-3.788 (-11.344 to 4.411)		
Week 9 (n=19,20)	-11.335 (-20.746 to -0.807)	-2.354 (-11.069 to 7.215)		
Week 13 (n=21,19)	-12.283 (-26.096 to 4.112)	-0.045 (-9.528 to 10.432)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Baseline in Estimated Glomerular Filtration Rate (eGFR) at Weeks 3, 5, 9 and 13

End point title	Percentage Change From Baseline in Estimated Glomerular Filtration Rate (eGFR) at Weeks 3, 5, 9 and 13

End point description:

The eGFR was calculated using 4 variable formula developed by the modification of diet in renal disease (MDRD) study group. The 4 variables needed to estimate glomerular filtration rate (GFR) using this formula were serum creatinine concentration, age, sex (for females, eGFR was multiplied by 0.742) and ethnic origin (for African-Caribbean people only, eGFR was multiplied by 1.212). Thus eGFR in milliliter per minute per 1.73 square meter (mL/min/1.73 m^2) = 175*(sCr/88.4)^-1.154*(Age)^-0.203*(0.742 if female)*(1.212 if African-Caribbean). Baseline eGFR was determined predose at Week 0 (Day 1). For Baseline eGFR, the "Low eGFR" group was defined as baseline eGFR < 45 mL/min/1.73m2, and the "High eGFR" group was defined as baseline eGFR > 45 mL/min/1.73 m2. FAS was defined as all enrolled subjects who had received at least one dose of study treatment and had at least one post-baseline measurement of UPCR based on 24-hour urine collected. n= subjects evaluable for specific timepoints.

End point type	Secondary

End point timeframe:

Baseline, Weeks 3, 5, 9 and 13

End point values	PF-06730512 1000 mg IV	PF-06730512 300 mg IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	24		
Units: Percent change				
least squares mean (confidence interval 90%)				
Week 3 (n=23,22)	5.657 (-0.722 to 12.446)	-0.180 (-4.179 to 3.987)		
Week 5 (n=21,23)	2.174 (-3.012 to 7.637)	-2.038 (-8.008 to 4.319)		
Week 9 (n=22,22)	-1.536 (-15.575 to 14.838)	-5.017 (-11.596 to 2.052)		
Week 13 (n=23,22)	2.892 (-6.096 to 12.740)	-12.217 (-18.831 to -5.063)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum PF-06730512 Concentration Versus Time Summary

End point title	Serum PF-06730512 Concentration Versus Time Summary

End point description:

The PK concentration analysis set was defined as all enrolled subjects treated who received at least one dose of PF-06730512 and had at least 1 measurable concentration. Here, 'Number Analyzed' signifies number of subjects evaluable for the specific rows. Here, '99999' indicates data could not be estimated as only one subject was evaluated.

End point type	Secondary

End point timeframe:

30 minutes pre-dose on Day 1, 8, 15, 29, 43, 57, 71, 85, 99, 113, 127, 141, 155, 169, follow-up (Fup) visit on Day 99, 113, 141, 183, 197, 225 and 1 hour post-dose on Day 1, 71, 155

End point values	PF-06730512 1000 mg IV	PF-06730512 300 mg IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	24		
Units: Microgram per millilitre				
arithmetic mean (standard deviation)				
Day 1 (n=17,22)	279.4 (± 86.548)	71.94 (± 29.668)		
Day 8 (n=1,10)	39.50 (± 99999)	13.09 (± 6.9363)		
Day 15 (n=23,21)	16.45 (± 11.266)	5.096 (± 3.1184)		
Day 29 (n=21,19)	24.92 (± 20.256)	6.916 (± 5.0154)		
Day 43 (n=20,19)	29.96 (± 22.062)	6.991 (± 5.5862)		
Day 57 (n=21,18)	32.56 (± 23.031)	7.664 (± 6.1325)		

Day 71 (n=17,17)	27.32 (± 16.688)	6.736 (± 5.6237)		
Day 85 (n=4,13)	41.15 (± 23.516)	7.597 (± 6.9184)		
Day 99/Fup (n=19,7)	11.50 (± 12.948)	2.313 (± 3.1827)		
Day 113/Fup (n=19,7)	4.991 (± 6.1121)	0.6356 (± 0.81118)		
Day 141/Fup (n=18,7)	1.385 (± 2.1196)	0.1438 (± 0.21666)		
Day 99 (n=4,9)	35.65 (± 16.065)	7.084 (± 6.9224)		
Day 113 (n=4,6)	42.40 (± 25.049)	9.442 (± 8.6965)		
Day 127 (n=3,6)	30.67 (± 5.3463)	6.732 (± 5.2295)		
Day 141 (n=4,7)	38.00 (± 13.880)	8.957 (± 10.753)		
Day 155 (n=3,8)	32.57 (± 5.8287)	7.585 (± 8.1601)		
Day 169 (n=4,16)	29.32 (± 15.338)	7.989 (± 7.4740)		
Day 183/Fup (n=4,16)	25.79 (± 30.417)	3.046 (± 3.8895)		
Day 197/Fup (n=4,16)	6.108 (± 4.0049)	1.048 (± 1.4978)		
Day 225/Fup (n=4,16)	2.009 (± 1.6808)	0.2659 (± 0.45714)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Positive Anti-Drug Antibody (ADA) and/or Neutralizing Antibody(NAb)

End point title	Number of Subjects With Positive Anti-Drug Antibody (ADA) and/or Neutralizing Antibody(NAb)

End point description:

The immunogenicity analysis population included all treated subjects with at least 1 ADA sample (pre-dose or post-treatment) analysed. Subjects those had only pre-dose baseline data and no post-treatment immunogenicity data, was not evaluated for subject-level ADA. Here, 'Number Analyzed' signifies number of subjects evaluable for the specific rows.

End point type	Secondary

End point timeframe:

From Day 1 of treatment up to Week 33

End point values	PF-06730512 1000 mg IV	PF-06730512 300 mg IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	24		
Units: Subjects				
ADA Positive (n=21,24)	1	0		
NAb Positive (n=21,24)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day 1 of treatment up to 9 weeks after last dose of study treatment (up to Week 33)

Adverse event reporting additional description:

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

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	PF-06730512 300 mg IV

Reporting group description:

Subjects received PF-06730512 300 mg IV Q2W.

Reporting group title	PF-06730512 1000 mg IV

Reporting group description:

Subjects received PF-06730512 1000 mg IV Q2W.

Serious adverse events	PF-06730512 300 mg IV	PF-06730512 1000 mg IV	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 24 (8.33%)	2 / 23 (8.70%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal impairment			

subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypervolaemia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	PF-06730512 300 mg IV	PF-06730512 1000 mg IV	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 24 (50.00%)	11 / 23 (47.83%)	
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	2 / 24 (8.33%)	2 / 23 (8.70%)	
occurrences (all)	2	2	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	2 / 24 (8.33%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 24 (12.50%)	2 / 23 (8.70%)	
occurrences (all)	3	3	

Dizziness			
subjects affected / exposed	2 / 24 (8.33%)	0 / 23 (0.00%)	
occurrences (all)	3	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 24 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Oedema			
subjects affected / exposed	2 / 24 (8.33%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Fatigue			
subjects affected / exposed	2 / 24 (8.33%)	3 / 23 (13.04%)	
occurrences (all)	2	4	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 24 (8.33%)	1 / 23 (4.35%)	
occurrences (all)	3	1	
Vomiting			
subjects affected / exposed	1 / 24 (4.17%)	2 / 23 (8.70%)	
occurrences (all)	2	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 24 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 24 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	2 / 24 (8.33%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Flank pain			
subjects affected / exposed	2 / 24 (8.33%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			

Urinary tract infection subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 3	0 / 23 (0.00%) 0	
Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2	0 / 23 (0.00%) 0	
COVID-19 subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2	1 / 23 (4.35%) 1	
Viral infection subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	2 / 23 (8.70%) 2	
Metabolism and nutrition disorders Dehydration subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	2 / 23 (8.70%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 May 2018	Specifications for dose levels, dosing frequency and route of administration have been included. Randomisation of subjects to the high versus the low dose has been removed. Instead, a sequential design has been implemented allowing Cohort 1 enrollment to complete prior to enrolment of Cohort 2.
10 June 2019	Changes in Inclusion and Exclusion Criteria and addition of the optional renal biopsy sub-study.
03 January 2020	Changes to Inclusion/Exclusion criteria.
12 June 2020	Revision/Clarification to contraception language for EU member states and Japan.
18 August 2021	The purpose of this amendment was to extend treatment duration from 12 weeks to 24 weeks, and to add an optional cohort to potentially explore a higher dose.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported