Clinical trial results:
A Phase 2a, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging, Parallel Group Study to Evaluate Safety, Tolerability, and Pharmacodynamics of PF-05221304 Administered Daily for 16-Weeks to Adult Subjects With Nonalcoholic Fatty Liver Disease

Summary

EudraCT number	2017-001156-55
Trial protocol	PL
Global end of trial date	27 March 2019

Results information

Result version number	v1 (current)
This version publication date	29 January 2021
First version publication date	29 January 2021

Trial information

Trial identification

Sponsor protocol code	C1171002

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc, +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc, +1 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	14 October 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 February 2019
Global end of trial reached?	Yes
Global end of trial date	27 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study was designed as a dose-ranging trial with placebo and 4 active doses of PF-05221304 to assess the safety, tolerability and the effect of PF-05221304 on liver fat.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 August 2017
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	Australia: 11
Country: Number of subjects enrolled	Canada: 56
Country: Number of subjects enrolled	Israel: 25
Country: Number of subjects enrolled	Poland: 69
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	United States: 138
Worldwide total number of subjects	305
EEA total number of subjects	69

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)	242
From 65 to 84 years	63
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This was a randomized, double-blind, placebo-controlled, 5 arm (placebo, plus 4 active doses of PF-05221304), parallel group study. A total of 305 subjects were assigned to study treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo matched to PF-05221304 tablet was administered orally once daily (QD) for up to 16 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo matching PF-05221304 tablet strengths of 1 mg and 5 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2 tablets orally QD for up to 16 weeks.

Investigational medicinal product name	Placebo matching PF-05221304 tablet strengths of 25 mg and 50 mg.
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet orally QD for up to 16 weeks.

Arm title	PF-05221304 2 mg

Arm description:

PF-05221304 tablet was administered orally at 2 mg QD for up to 16 weeks.

Arm type	Experimental
Investigational medicinal product name	PF-05221304
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 mg PF-05221304 tablet 2 tables orally QD for up to 16 weeks.

Arm title	PF-05221304 10 mg

Arm description:	
PF-05221304 tablet was administered orally at 10 mg QD for up to 16 weeks.	
Arm type	Experimental
Investigational medicinal product name	PF-05221304
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
5 mg PF-05221304 tablet 2 tablets orally QD for up to 16 weeks.	
Arm title	PF-05221304 25 mg
Arm description:	
PF-05221304 tablet was administered orally at 25 mg QD for up to 16 weeks.	
Arm type	Experimental
Investigational medicinal product name	PF-05221304
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
25 mg PF-05221304 tablet 1 tablet orally QD for up to 16 weeks.	
Arm title	PF-05221304 50 mg
Arm description:	
PF-05221304 tablet was administered orally at 50 mg QD for up to 16 weeks.	
Arm type	Experimental
Investigational medicinal product name	PF-05221304
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
50 mg PF-05221304 tablet 1 tablet orally QD for up to 16 weeks.	

Number of subjects in period 1	Placebo	PF-05221304 2 mg	PF-05221304 10 mg
Started	61	63	62
Completed	54	58	55
Not completed	7	5	7
Consent withdrawn by subject	2	2	3
Adverse event, non-fatal	3	3	2
Lost to follow-up	-	-	-
Protocol deviation	2	-	2

Number of subjects in period 1	PF-05221304 25 mg	PF-05221304 50 mg
Started	58	61

Completed	48	48
Not completed	10	13
Consent withdrawn by subject	4	2
Adverse event, non-fatal	6	9
Lost to follow-up	-	1
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	305	305	
Age Categorical Units: Subjects			
Adults (18-44 years)	65	65	
Adults (45-64 years)	177	177	
Adults (>=65 years)	63	63	
Age Continuous Units: years			
geometric mean	53.38		
standard deviation	± 11.99	-	
Gender Categorical Units: Subjects			
Female	171	171	
Male	134	134	
Race/Ethnicity Units: Subjects			
White	252	252	
Black or African American	4	4	
Asian	38	38	
American Indian or Alaska Native	1	1	
Native Hawaiian or Other Pacific Islander	1	1	
Not Reported	9	9	

Subject analysis sets	
Subject analysis set title	Placebo
Subject analysis set type	Per protocol
Subject analysis set description: Subjects who received PF-05221304 tablet orally at 2/10/25/50 mg QD for up to 16 weeks.	
Subject analysis set title	PF-05221304 2 mg
Subject analysis set type	Per protocol
Subject analysis set description: Subjects who received PF-05221304 tablet orally at 2/10/25/50 mg QD for up to 16 weeks.	
Subject analysis set title	PF-05221304 10 mg
Subject analysis set type	Per protocol
Subject analysis set description: Subjects who received PF-05221304 tablet orally at 2/10/25/50 mg QD for up to 16 weeks.	
Subject analysis set title	PF-05221304 25 mg
Subject analysis set type	Per protocol
Subject analysis set description: Subjects who received PF-05221304 tablet orally at 2/10/25/50 mg QD for up to 16 weeks.	

Subject analysis set title	PF-05221304 50 mg
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects who received PF-05221304 tablet orally at 2/10/25/50 mg QD for up to 16 weeks.

Reporting group values	Placebo	PF-05221304 2 mg	PF-05221304 10 mg
Number of subjects	61	63	62
Age Categorical Units: Subjects			
Adults (18-44 years)	12	10	18
Adults (45-64 years)	40	41	29
Adults (>=65 years)	9	12	15
Age Continuous Units: years			
geometric mean	53.33	54.10	52.66
standard deviation	± 10.77	± 11.86	± 12.75
Gender Categorical Units: Subjects			
Female	36	37	33
Male	25	26	29
Race/Ethnicity Units: Subjects			
White	53	50	52
Black or African American	1	1	1
Asian	5	7	7
American Indian or Alaska Native	0	1	0
Native Hawaiian or Other Pacific Islander	0	1	0
Not Reported	2	3	2

Reporting group values	PF-05221304 25 mg	PF-05221304 50 mg	
Number of subjects	58	61	
Age Categorical Units: Subjects			
Adults (18-44 years)	12	13	
Adults (45-64 years)	34	33	
Adults (>=65 years)	12	15	
Age Continuous Units: years			
geometric mean	54.02	52.82	
standard deviation	± 11.58	± 13.12	
Gender Categorical Units: Subjects			
Female	35	30	
Male	23	31	
Race/Ethnicity Units: Subjects			
White	46	51	
Black or African American	1	0	
Asian	9	10	
American Indian or Alaska Native	0	0	

Native Hawaiian or Other Pacific Islander	0	0	
Not Reported	2	0	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo matched to PF-05221304 tablet was administered orally once daily (QD) for up to 16 weeks.	
Reporting group title	PF-05221304 2 mg
Reporting group description:	
PF-05221304 tablet was administered orally at 2 mg QD for up to 16 weeks.	
Reporting group title	PF-05221304 10 mg
Reporting group description:	
PF-05221304 tablet was administered orally at 10 mg QD for up to 16 weeks.	
Reporting group title	PF-05221304 25 mg
Reporting group description:	
PF-05221304 tablet was administered orally at 25 mg QD for up to 16 weeks.	
Reporting group title	PF-05221304 50 mg
Reporting group description:	
PF-05221304 tablet was administered orally at 50 mg QD for up to 16 weeks.	
Subject analysis set title	Placebo
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects who received PF-05221304 tablet orally at 2/10/25/50 mg QD for up to 16 weeks.	
Subject analysis set title	PF-05221304 2 mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects who received PF-05221304 tablet orally at 2/10/25/50 mg QD for up to 16 weeks.	
Subject analysis set title	PF-05221304 10 mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects who received PF-05221304 tablet orally at 2/10/25/50 mg QD for up to 16 weeks.	
Subject analysis set title	PF-05221304 25 mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects who received PF-05221304 tablet orally at 2/10/25/50 mg QD for up to 16 weeks.	
Subject analysis set title	PF-05221304 50 mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects who received PF-05221304 tablet orally at 2/10/25/50 mg QD for up to 16 weeks.	

Primary: Percent Change from Baseline in Liver Fat by Magnetic Resonance Imaging-Proton Density Fat Fraction (MRI- PDFF) at Week 16

End point title	Percent Change from Baseline in Liver Fat by Magnetic Resonance Imaging-Proton Density Fat Fraction (MRI- PDFF) at Week 16
End point description:	
MRI-PDFF utilized a gradient echo sequence with low flip angle (FA) to minimize T1 bias, corrected T2* decay (due to iron overload) via modeling of the fat signal as a superposition of multiple frequency components from 5 different lipid types, and was applied in each of the 9 Couinaud segments. This technique improved fat quantification accuracy for the entire liver permitting quantification of small differences/changes following pharmacological intervention. All randomized subjects who received at least 1 dose of randomized study treatment and with non-missing baseline and post-baseline endpoint.	
End point type	Primary

End point timeframe:
Baseline (between Day -14 and Day 1), Week 16

End point values	Placebo	PF-05221304 2 mg	PF-05221304 10 mg	PF-05221304 25 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	59	57	54
Units: Percent change				
least squares mean (confidence interval 80%)	-7.2 (-13.9 to 0.0)	-17.1 (-22.7 to -11.1)	-49.9 (-53.3 to -46.2)	-55.9 (-59.0 to -52.4)

End point values	PF-05221304 50 mg			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: Percent change				
least squares mean (confidence interval 80%)	-64.8 (-67.5 to -62.0)			

Statistical analyses

Statistical analysis title	Placebo, PF-05221304
Comparison groups	Placebo v PF-05221304 2 mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (net)
Point estimate	-10.7
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-19.4
upper limit	-1.1

Statistical analysis title	Placebo, PF-05221304 10 mg
Comparison groups	Placebo v PF-05221304 10 mg
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (net)
Point estimate	-46

Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-51.3
upper limit	-40.1

Statistical analysis title	Placebo, PF-05221304 25 mg
Comparison groups	Placebo v PF-05221304 25 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (net)
Point estimate	-52.4
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-57.2
upper limit	-47.1

Statistical analysis title	Placebo, PF-05221304 50 mg
Comparison groups	Placebo v PF-05221304 50 mg
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (net)
Point estimate	-62.1
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-66
upper limit	-57.8

Secondary: Percent Change from Baseline in Alanine Aminotransferase at Week 16	
End point title	Percent Change from Baseline in Alanine Aminotransferase at Week 16
End point description:	
Potential improvement in liver function was denoted by reduction in alanine transaminase (ALT). All randomized subjects who received at least 1 dose of randomized study treatment and diagnosed/presumed with nonalcoholic steatohepatitis.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1 pre-dose), Week 16	

End point values	Placebo	PF-05221304 2 mg	PF-05221304 10 mg	PF-05221304 25 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	42	42	39
Units: Percent change				
least squares mean (confidence interval 80%)	-8.5 (-15.2 to -1.2)	-12.5 (-18.7 to -5.8)	-27.7 (-32.9 to -22.2)	-31.3 (-36.6 to -25.5)

End point values	PF-05221304 50 mg			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Percent change				
least squares mean (confidence interval 80%)	-46.8 (-50.8 to -42.4)			

Statistical analyses

Statistical analysis title	Placebo, PF-05221304 2 mg
Comparison groups	Placebo v PF-05221304 2 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (net)
Point estimate	-4.4
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-14
upper limit	6.3

Statistical analysis title	Placebo, PF-05221304 10 mg
Comparison groups	Placebo v PF-05221304 10 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (net)
Point estimate	-21

Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-29
upper limit	-12.2

Statistical analysis title	Placebo, PF-05221304 25 mg
Comparison groups	Placebo v PF-05221304 25 mg
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (net)
Point estimate	-25
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-32.8
upper limit	-16.1

Statistical analysis title	Placebo, PF-05221304 50 mg
Comparison groups	Placebo v PF-05221304 50 mg
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (net)
Point estimate	-41.8
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-47.9
upper limit	-35

Secondary: Number of Subjects With Treatment-Emergent Adverse Events

End point title	Number of Subjects With Treatment-Emergent Adverse Events

End point description:

An adverse event (AE) was any untoward medical occurrence in a study subject administered a product or medical device. A serious AE (SAE) is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; lifethreatening; initial or prolonged inpatient hospitalization; persistent or significant disability/incapacity; congenital anomaly/birth defect. Any such events with initial onset or increasing in severity after the first dose of study treatment were counted as treatment-emergent. All randomized subjects who received at least 1 dose of randomized study treatment.

End point type	Secondary

End point timeframe:

From first dose of study treatment (Day 1) up to Week 20

End point values	Placebo	PF-05221304 2 mg	PF-05221304 10 mg	PF-05221304 25 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	63	62	58
Units: Subjects				
All-causality AE	41	40	42	45
All-causality SAE	0	1	1	2
Treatment-related AE	16	9	12	16
Treatment-related SAE	0	0	0	0

End point values	PF-05221304 50 mg			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Subjects				
All-causality AE	40			
All-causality SAE	2			
Treatment-related AE	23			
Treatment-related SAE	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Laboratory Abnormalities

End point title	Number of Subjects With Laboratory Abnormalities

End point description:

Following laboratory parameters were assessed against pre-defined abnormality criteria: hematology (hemoglobin, hematocrit, erythrocytes, reticulocytes, platelets, leukocytes, lymphocytes, neutrophils, basophils, eosinophils, monocytes, activated partial thromboplastin time, prothrombin time [PT], PT/international normalized ratio, reticulocytes); chemistry (indirect bilirubin, direct bilirubin, protein, albumin, blood urea nitrogen, creatinine, creatine kinase, urate, calcium, sodium, potassium, chloride, bicarbonate, urine urobilinogen); urinalysis (pH, urine glucose, urine ketones, urine protein, urine hemoglobin, nitrites, leukocyte esterase, urine erythrocytes, urine leukocytes, urine hyaline casts, urine bilirubin, granular casts). All randomized subjects who received at least 1 dose of randomized study treatment and had laboratory data.

End point type	Secondary

End point timeframe:

From first dose of study treatment (Day 1) up to Week 20

End point values	Placebo	PF-05221304 2 mg	PF-05221304 10 mg	PF-05221304 25 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	63	62	58
Units: Subjects				
With Laboratory Abnormalities	39	44	36	33

End point values	PF-05221304 50 mg			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Subjects				
With Laboratory Abnormalities	40			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Vital Signs Data Meeting Predefined Criteria

End point title	Number of Subjects With Vital Signs Data Meeting Predefined Criteria

End point description:

Vital signs categorical summarization criteria: 1) sitting systolic blood pressure (SBP) <90 or >180 millimeters of mercury (mmHg); 2) sitting diastolic blood pressure (DBP) <50 mmHg or >110 mmHg; 3) sitting pulse rate <40 or >120 beats per minute (bpm); 4) change from baseline (increase or decrease) in sitting DBP greater than or equal to (>=) 20 mmHg; 5) change from baseline (increase or decrease) in sitting SBP >=30 mmHg. All randomized subjects who received at least 1 dose of randomized study treatment and had vital signs data.

End point type	Secondary

End point timeframe:

From first dose of study treatment (Day 1) up to Week 18

End point values	Placebo	PF-05221304 2 mg	PF-05221304 10 mg	PF-05221304 25 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	63	62	58
Units: Subjects				
Sitting SBP <90 mmHg	0	0	0	0
Sitting SBP >180 mmHg	0	0	0	1
Sitting SBP increase >=30 mmHg	5	6	2	2
Sitting SBP decrease >=30 mmHg	2	1	5	7
Sitting DBP >110 mmHg	0	0	0	0
Sitting DBP increase >=20 mmHg	1	4	2	2
Sitting DBP decrease >=20 mmHg	0	4	3	4
Sitting pulse rate <40 bpm	0	0	0	0
Sitting pulse rate >120 bpm	0	0	0	0

Sitting DBP <50 mmHg	1	0	0	0

End point values	PF-05221304 50 mg			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Subjects				
Sitting SBP <90 mmHg	2			
Sitting SBP >180 mmHg	0			
Sitting SBP increase >=30 mmHg	0			
Sitting SBP decrease >=30 mmHg	6			
Sitting DBP >110 mmHg	1			
Sitting DBP increase >=20 mmHg	3			
Sitting DBP decrease >=20 mmHg	4			
Sitting pulse rate <40 bpm	0			
Sitting pulse rate >120 bpm	0			
Sitting DBP <50 mmHg	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With 12-Lead Electrocardiogram (ECG) Data Meeting Predefined Criteria

End point title	Number of Subjects With 12-Lead Electrocardiogram (ECG) Data Meeting Predefined Criteria

End point description:

ECG categorical summarization criteria 1.QRS interval (time from ECG Q wave to end of S wave corresponding to ventricle depolarization) >=140msec 2.QRS interval >=50% change from baseline 3.PR interval (interval between start of P wave and start of QRS complex, corresponding to time between onset of atrial depolarization and onset of ventricular depolarization) >=300msec 4.PR interval >=25% change when baseline is >200msec or >=50% change when baseline is <=200msec 5.QT interval (time from ECG Q wave to end of T wave corresponding to electrical systole): absolute value of >=500msec 6.QTcF interval (QT corrected for heart rate using Fridericia's formula) absolute value of 450 to <480msec 7.QTcF interval: absolute value of 480 to <500msec 8.QTcF interval: absolute value >=500msec 9.QTcF interval: a change from baseline of 30 to <60msec 10.QTcF interval: a change from baseline >=60 msec. All randomized subjects who received at least 1 dose of randomized study treatment and had ECG data

End point type	Secondary

End point timeframe:

From first dose of study treatment (Day 1) up to Week 18

End point values	Placebo	PF-05221304 2 mg	PF-05221304 10 mg	PF-05221304 25 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	63	61	58
Units: Subjects				
PR interval >=300 msec	0	0	0	0
%Change in PR interval >=25/50%	0	1	0	1
QRS interval >=140 msec	0	0	1	0
%Change in QRS interval >=50%	0	0	0	0
QT interval >=500 msec	0	0	0	1
QTcF interval >=450 to <480 msec	6	10	7	9
QTcF interval >=480 to <500 msec	0	1	0	1
QTcF interval >=500 msec	0	0	0	0
QTcF interval increase >=30 to 60 msec	5	6	8	10
QTcF interval increase >=60 msec	2	1	0	0

End point values	PF-05221304 50 mg			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Subjects				
PR interval >=300 msec	0			
%Change in PR interval >=25/50%	1			
QRS interval >=140 msec	0			
%Change in QRS interval >=50%	0			
QT interval >=500 msec	0			
QTcF interval >=450 to <480 msec	3			
QTcF interval >=480 to <500 msec	1			
QTcF interval >=500 msec	0			
QTcF interval increase >=30 to 60 msec	4			
QTcF interval increase >=60 msec	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study treatment up to 20 weeks.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Placebo matched to PF-05221304 tablet was administered orally once daily (QD) for up to 16 weeks.

Reporting group title	PF-05221304 2 mg

Reporting group description:

PF-05221304 tablet was administered orally at 2 mg QD for up to 16 weeks.

Reporting group title	PF-05221304 10 mg

Reporting group description:

PF-05221304 tablet was administered orally at 10 mg QD for up to 16 weeks.

Reporting group title	PF-05221304 25 mg

Reporting group description:

PF-05221304 tablet was administered orally at 25 mg QD for up to 16 weeks.

Reporting group title	PF-05221304 50 mg

Reporting group description:

PF-05221304 tablet was administered orally at 50 mg QD for up to 16 weeks.

Serious adverse events	Placebo	PF-05221304 2 mg	PF-05221304 10 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 61 (0.00%)	1 / 63 (1.59%)	1 / 62 (1.61%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Rib fissure	Additional description: Rib fracture		
subjects affected / exposed	0 / 61 (0.00%)	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina	Additional description: Angina unstable		
subjects affected / exposed	0 / 61 (0.00%)	0 / 63 (0.00%)	0 / 62 (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

Myocardial infarct			
subjects affected / exposed	0 / 61 (0.00%)	1 / 63 (1.59%)	0 / 62 (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
Myocardial ischemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 63 (0.00%)	0 / 62 (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
Respiratory, thoracic and mediastinal disorders			
Asthmatic			
subjects affected / exposed	0 / 61 (0.00%)	0 / 63 (0.00%)	0 / 62 (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
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 61 (0.00%)	0 / 63 (0.00%)	0 / 62 (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
Infections and infestations			
pneumonia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 63 (1.59%)	0 / 62 (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
upper respiratory tract infection			
subjects affected / exposed	0 / 61 (0.00%)	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	PF-05221304 25 mg	PF-05221304 50 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 58 (3.45%)	2 / 61 (3.28%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Rib fissure	Additional description: Rib fracture		

subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina	Additional description: Angina unstable		
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarct			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischemia			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthmatic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	
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 colic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
pneumonia			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
upper respiratory tract infection			

subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	PF-05221304 2 mg	PF-05221304 10 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 61 (44.26%)	21 / 63 (33.33%)	25 / 62 (40.32%)
Investigations			
Blood triglycerides increased			
subjects affected / exposed	0 / 61 (0.00%)	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 61 (6.56%)	3 / 63 (4.76%)	1 / 62 (1.61%)
occurrences (all)	4	3	2
Headache			
subjects affected / exposed	8 / 61 (13.11%)	3 / 63 (4.76%)	3 / 62 (4.84%)
occurrences (all)	10	3	4
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 61 (8.20%)	3 / 63 (4.76%)	2 / 62 (3.23%)
occurrences (all)	5	3	2
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 61 (1.64%)	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	1	0	1
Diarrhoea			
subjects affected / exposed	3 / 61 (4.92%)	3 / 63 (4.76%)	8 / 62 (12.90%)
occurrences (all)	3	4	12
Nausea			
subjects affected / exposed	3 / 61 (4.92%)	0 / 63 (0.00%)	3 / 62 (4.84%)
occurrences (all)	3	0	3
Skin and subcutaneous tissue disorders			

Pruritus			
subjects affected / exposed	1 / 61 (1.64%)	2 / 63 (3.17%)	0 / 62 (0.00%)
occurrences (all)	1	2	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 61 (1.64%)	1 / 63 (1.59%)	3 / 62 (4.84%)
occurrences (all)	1	1	3
Muscle spasms			
subjects affected / exposed	4 / 61 (6.56%)	0 / 63 (0.00%)	2 / 62 (3.23%)
occurrences (all)	4	0	2
Pain in extremity			
subjects affected / exposed	2 / 61 (3.28%)	3 / 63 (4.76%)	4 / 62 (6.45%)
occurrences (all)	2	3	4
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 61 (3.28%)	0 / 63 (0.00%)	3 / 62 (4.84%)
occurrences (all)	2	0	3
Upper respiratory tract infection			
subjects affected / exposed	2 / 61 (3.28%)	6 / 63 (9.52%)	3 / 62 (4.84%)
occurrences (all)	2	8	3
Urinary tract infection			
subjects affected / exposed	1 / 61 (1.64%)	1 / 63 (1.59%)	2 / 62 (3.23%)
occurrences (all)	1	1	2
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	2 / 61 (3.28%)	1 / 63 (1.59%)	6 / 62 (9.68%)
occurrences (all)	2	1	6

Non-serious adverse events	PF-05221304 25 mg	PF-05221304 50 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 58 (53.45%)	29 / 61 (47.54%)	
Investigations			
Blood triglycerides increased			
subjects affected / exposed	3 / 58 (5.17%)	2 / 61 (3.28%)	
occurrences (all)	3	3	
Nervous system disorders			

Dizziness			
subjects affected / exposed	3 / 58 (5.17%)	3 / 61 (4.92%)	
occurrences (all)	3	3	
Headache			
subjects affected / exposed	7 / 58 (12.07%)	4 / 61 (6.56%)	
occurrences (all)	7	5	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 58 (3.45%)	2 / 61 (3.28%)	
occurrences (all)	2	2	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	6 / 58 (10.34%)	1 / 61 (1.64%)	
occurrences (all)	7	1	
Diarrhoea			
subjects affected / exposed	2 / 58 (3.45%)	4 / 61 (6.56%)	
occurrences (all)	4	4	
Nausea			
subjects affected / exposed	5 / 58 (8.62%)	4 / 61 (6.56%)	
occurrences (all)	6	4	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 58 (5.17%)	1 / 61 (1.64%)	
occurrences (all)	3	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 58 (6.90%)	0 / 61 (0.00%)	
occurrences (all)	4	0	
Muscle spasms			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	2 / 58 (3.45%)	1 / 61 (1.64%)	
occurrences (all)	2	1	
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	3 / 58 (5.17%)	2 / 61 (3.28%)	
occurrences (all)	3	2	
Upper respiratory tract infection			
subjects affected / exposed	3 / 58 (5.17%)	2 / 61 (3.28%)	
occurrences (all)	3	2	
Urinary tract infection			
subjects affected / exposed	5 / 58 (8.62%)	4 / 61 (6.56%)	
occurrences (all)	5	4	
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	4 / 58 (6.90%)	10 / 61 (16.39%)	
occurrences (all)	4	12	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 July 2017	This amendment was making substantial changes as requested by the United States Food and Drug Administration (US FDA) as part of their review of the original protocol submitted on 11May2017.
03 October 2017	This amendment was making the substantial changes to align with the Pfizer Enterprise-level revision to appropriate measures to prevent pregnancy in the population of childbearing potential enrolled who are sexually active and align with the Clinical Trial Facilitation Group (CTFG) 2014 European Guidance.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported