Clinical trial results:
A Phase 2, Randomized, Double-Blind, Double-Dummy, Placebo-Controlled, Dose-Ranging, Dose-Finding, Parallel Group Study to Assess Efficacy and Safety of PF-06865571 (DGAT2I) Alone and When Coadministered With PF-05221304 (ACCI) in Adult Participants With Biopsy-Confirmed Nonalcoholic Steatohepatitis and Fibrosis Stage 2 or 3

Summary

EudraCT number	2019-004775-39
Trial protocol	PL SK BG
Global end of trial date	23 February 2024

Results information

Result version number	v1 (current)
This version publication date	02 March 2025
First version publication date	02 March 2025

Trial information

Trial identification

Sponsor protocol code	C2541013

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04321031
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	66 Hudson Boulevard East, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 May 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 February 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of a range of diacylglycerol acyltransferase 2 inhibitor (PF-06865571/DGAT2i) doses administered alone, and coadministration of DGAT2i + acetyl-CoA carboxylase inhibitor (PF-05221304/ACCi), compared to placebo, and the coadministration of DGAT2i + ACCi relative to DGAT2i alone, in participants with biopsy confirmed nonalcoholic steatohepatitis (NASH) and fibrosis, on resolution of NASH without worsening of fibrosis or improvement in fibrosis by greater than or equal to (>=) 1 stage without worsening of NASH, or both.

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 Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 June 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 1
Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	China: 4
Country: Number of subjects enrolled	Hong Kong: 14
Country: Number of subjects enrolled	India: 1
Country: Number of subjects enrolled	Japan: 45
Country: Number of subjects enrolled	Korea, Republic of: 8
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Puerto Rico: 15
Country: Number of subjects enrolled	Slovakia: 4
Country: Number of subjects enrolled	Taiwan: 5
Country: Number of subjects enrolled	United States: 145
Worldwide total number of subjects	255
EEA total number of subjects	8

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)	188
From 65 to 84 years	67
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 256 participants with biopsy confirmed Non-alcoholic Steatohepatitis (NASH) with fibrosis state (F2-F3) were randomized, of which 255 were treated.

Pre-assignment

Screening details:

F2: significant stage of fibrosis when scarring had occurred and extended outside liver area and F3: severe stage of fibrosis with spreading and forming bridges with other fibrotic liver areas.

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, Carer, Assessor

Blinding implementation details:

Double blind, double dummy, placebo controlled.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants were randomised to receive 2 tablets of DGAT2i matching placebo and 1 tablet of ACCi matching placebo twice a day (BID) for 48 weeks by oral administration. Participants were followed up to 52 weeks.

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

Dosage and administration details:

Participants received 2 tablets of DGAT2i matching placebo and 1 tablet of ACCi matching placebo orally BID for 48 weeks.

Arm title	DGAT2i/PF-06865571 25 mg BID

Arm description:

Participants were randomised to receive 1 tablet of DGAT2i 25 milligrams (mg) along with 1 tablet of DGAT2i and ACCi matching placebo BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	DGAT2i
Investigational medicinal product code	PF-06865571
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 1 tablet of DGAT2i 25 mg along with 1 tablet of DGAT2i and ACCi matching placebos orally BID for 48 weeks.

Arm title	DGAT2i/PF-06865571 75 mg BID

Arm description:

Participants were randomised to receive 1 tablet of DGAT2i 25 mg, 1 tablet of DGAT2i 50 mg and 1

tablet of ACCi matching placebo BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	DGAT2i
Investigational medicinal product code	PF-06865571
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 1 tablet of DGAT2i 25 mg, 1 tablet of DGAT2i 50 mg and 1 tablet of ACCi matching placebo orally BID for 48 weeks.

Arm title	DGAT2i/PF-06865571 150 mg BID

Arm description:

Participants were randomised to receive 1 tablet of DGAT2i matching placebo, 1 tablet of DGAT2i 150 mg and 1 tablet of ACCi matching placebo BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	DGAT2i
Investigational medicinal product code	PF-06865571
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 1 tablet of DGAT2i matching placebo, 1 tablet of DGAT2i 150 mg and 1 tablet of ACCi matching placebo orally BID for 48 weeks.

Arm title	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID

Arm description:

Participants were randomised to receive 1 tablet of DGAT2i matching placebo, 1 tablet of DGAT2i 150 mg and 1 tablet of ACCi 5 mg BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	DGAT2i + ACCi
Investigational medicinal product code	PF-06865571 + PF-05221304
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 1 tablet of DGAT2i matching placebo, 1 tablet of DGAT2i 150 mg and 1 tablet of ACCi 5 mg orally BID for 48 weeks.

Arm title	DGAT2i/PF-06865571 300 mg BID

Arm description:

Participants were randomised to receive 2 tablets of DGAT2i 150 mg and 1 tablet of ACCi matching placebo BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	DGAT2i
Investigational medicinal product code	PF-06865571
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets of DGAT2i 150 mg and 1 tablet of ACCi matching placebo orally BID for 48 weeks.

Arm title	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID

Arm description:

Participants were randomised to receive 2 tablets of DGAT2i 150 mg and 1 tablet of ACCi 10 mg BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	DGAT2i + ACCi
Investigational medicinal product code	PF-06865571 + PF-05221304
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets of DGAT2i 150 mg and 1 tablet of ACCi 10 mg orally BID for 48 weeks.

Number of subjects in period 1	Placebo	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID
Started	34	35	48
Completed	32	31	45
Not completed	2	4	3
Consent withdrawn by subject	2	2	1
Adverse event, non-fatal	-	2	2
Non-compliance with study drug	-	-	-
Unspecified	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	DGAT2i/PF-06865571 150 mg BID	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID	DGAT2i/PF-06865571 300 mg BID
Started	42	35	31
Completed	35	32	26
Not completed	7	3	5
Consent withdrawn by subject	3	1	-
Adverse event, non-fatal	2	2	2
Non-compliance with study drug	-	-	1
Unspecified	1	-	-
Lost to follow-up	1	-	2

Number of subjects in period 1	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID
Started	30
Completed	28
Not completed	2
Consent withdrawn by subject	1
Adverse event, non-fatal	-

Non-compliance with study drug	-
Unspecified	-
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants were randomised to receive 2 tablets of DGAT2i matching placebo and 1 tablet of ACCi matching placebo twice a day (BID) for 48 weeks by oral administration. Participants were followed up to 52 weeks.	
Reporting group title	DGAT2i/PF-06865571 25 mg BID
Reporting group description:	
Participants were randomised to receive 1 tablet of DGAT2i 25 milligrams (mg) along with 1 tablet of DGAT2i and ACCi matching placebo BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.	
Reporting group title	DGAT2i/PF-06865571 75 mg BID
Reporting group description:	
Participants were randomised to receive 1 tablet of DGAT2i 25 mg, 1 tablet of DGAT2i 50 mg and 1 tablet of ACCi matching placebo BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.	
Reporting group title	DGAT2i/PF-06865571 150 mg BID
Reporting group description:	
Participants were randomised to receive 1 tablet of DGAT2i matching placebo, 1 tablet of DGAT2i 150 mg and 1 tablet of ACCi matching placebo BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.	
Reporting group title	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID
Reporting group description:	
Participants were randomised to receive 1 tablet of DGAT2i matching placebo, 1 tablet of DGAT2i 150 mg and 1 tablet of ACCi 5 mg BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.	
Reporting group title	DGAT2i/PF-06865571 300 mg BID
Reporting group description:	
Participants were randomised to receive 2 tablets of DGAT2i 150 mg and 1 tablet of ACCi matching placebo BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.	
Reporting group title	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID
Reporting group description:	
Participants were randomised to receive 2 tablets of DGAT2i 150 mg and 1 tablet of ACCi 10 mg BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.	

Reporting group values	Placebo	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID
Number of subjects	34	35	48
Age categorical Units: Subjects			
In Utero	0	0	0
Preterm newborn infants (gestional age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days - 23 months)	0	0	0
Children (2 - 11 years)	0	0	0
12 - 17 years	0	0	0
Adults (18 - 64 years)	25	27	33
From 65 - 84 years	9	8	15

85 years and over	0	0	0

Age continuous Units: years			
arithmetic mean	55.21	56.54	56.02
standard deviation	± 12.00	± 11.38	± 12.67
Sex: Female, Male Units: Subjects			
Male	17	16	17
Female	17	19	31
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	12	10	16
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	2	0
White	21	20	31
More than one race	0	0	0
Unknown or Not Reported	1	3	1
Ethnicity Units: Subjects			
Hispanic or Latino	8	15	13
Not Hispanic or Latino	24	20	35
Unknown or Not Reported	2	0	0

Reporting group values	DGAT2i/PF-06865571 150 mg BID	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID	DGAT2i/PF-06865571 300 mg BID
Number of subjects	42	35	31
Age categorical Units: Subjects			
In Utero	0	0	0
Preterm newborn infants (gestional age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days - 23 months)	0	0	0
Children (2 - 11 years)	0	0	0
12 - 17 years	0	0	0
Adults (18 - 64 years)	29	26	23
From 65 - 84 years	13	9	8
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	55.95	56.60	59.65
standard deviation	± 11.32	± 10.23	± 7.49
Sex: Female, Male Units: Subjects			
Male	14	11	11
Female	28	24	20

Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	14	13	11
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	1
White	24	19	17
More than one race	0	0	0
Unknown or Not Reported	3	2	2
Ethnicity Units: Subjects			
Hispanic or Latino	10	6	11
Not Hispanic or Latino	29	29	18
Unknown or Not Reported	3	0	2

Reporting group values	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID	Total	
Number of subjects	30	255	
Age categorical Units: Subjects			
In Utero	0	0	
Preterm newborn infants (gestional 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	
12 - 17 years	0	0	
Adults (18 - 64 years)	25	188	
From 65 - 84 years	5	67	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	54.23		
standard deviation	± 11.32	-	
Sex: Female, Male Units: Subjects			
Male	15	101	
Female	15	154	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	11	87	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	5	
White	18	150	
More than one race	0	0	
Unknown or Not Reported	1	13	
Ethnicity			

Units: Subjects			
Hispanic or Latino	8	71	
Not Hispanic or Latino	20	175	
Unknown or Not Reported	2	9	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants were randomised to receive 2 tablets of DGAT2i matching placebo and 1 tablet of ACCi matching placebo twice a day (BID) for 48 weeks by oral administration. Participants were followed up to 52 weeks.	
Reporting group title	DGAT2i/PF-06865571 25 mg BID
Reporting group description:	
Participants were randomised to receive 1 tablet of DGAT2i 25 milligrams (mg) along with 1 tablet of DGAT2i and ACCi matching placebo BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.	
Reporting group title	DGAT2i/PF-06865571 75 mg BID
Reporting group description:	
Participants were randomised to receive 1 tablet of DGAT2i 25 mg, 1 tablet of DGAT2i 50 mg and 1 tablet of ACCi matching placebo BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.	
Reporting group title	DGAT2i/PF-06865571 150 mg BID
Reporting group description:	
Participants were randomised to receive 1 tablet of DGAT2i matching placebo, 1 tablet of DGAT2i 150 mg and 1 tablet of ACCi matching placebo BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.	
Reporting group title	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID
Reporting group description:	
Participants were randomised to receive 1 tablet of DGAT2i matching placebo, 1 tablet of DGAT2i 150 mg and 1 tablet of ACCi 5 mg BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.	
Reporting group title	DGAT2i/PF-06865571 300 mg BID
Reporting group description:	
Participants were randomised to receive 2 tablets of DGAT2i 150 mg and 1 tablet of ACCi matching placebo BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.	
Reporting group title	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID
Reporting group description:	
Participants were randomised to receive 2 tablets of DGAT2i 150 mg and 1 tablet of ACCi 10 mg BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.	

Primary: Mean Proportion of Participants Achieving Resolution of NASH Without Worsening or Improvement of Fibrosis by >=1 Stage Without Worsening of NASH or Both Based on Assessment by Sponsor-Identified Central Pathologist at Week 48: Bayesian Dose Response Model

End point title	Mean Proportion of Participants Achieving Resolution of NASH Without Worsening or Improvement of Fibrosis by >=1 Stage Without Worsening of NASH or Both Based on Assessment by Sponsor-Identified Central Pathologist at Week 48: Bayesian Dose Response Model[1]

End point description:

NASH resolution: disappearance of ballooning (NAS ballooning score=0; 0=no ballooning, 1= few balloon cells, 2= many cells, prominent ballooning; HS= more DA), residual/no LI (NAS LI score 0/1, 0= no foci, 1= <2 foci, 2= 2-4 foci, 3= >4 foci; HS = more DA), NAS steatosis score 0, 1, 2 or 3, 0= <5% hepatocytes involved (HI), 1= 5-33% HI, 2= 34-66% HI, 3= >66% HI; HS= more DA. No worsening of fibrosis: no change/decrease of 1 stage in BKS CTB. Improvement in fibrosis by>=1 stage: decrease of 1 stage in BKS CTB. No worsening of NASH: no change/increase in NAS for ballooning, inflammation, steatosis CTB. CI indicated credible interval below. BKS: scaling for fibrosis (0= none, 1= perisinusoidal/

periportal, 2= perisinusoidal, portal/ periportal, 3=bridging, 4= cirrhosis; higher scores= more DA). FAS was analysed. Endpoint was not planned in combination arms.

End point type	Primary

End point timeframe:

Week 48

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is reporting statistics for the arms specified

End point values	Placebo	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID	DGAT2i/PF-06865571 150 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	35	48	42
Units: Proportion of participants				
arithmetic mean (confidence interval 90%)	0.38 (0.26 to 0.50)	0.45 (0.38 to 0.53)	0.48 (0.42 to 0.55)	0.50 (0.43 to 0.57)

End point values	DGAT2i/PF-06865571 300 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: Proportion of participants				
arithmetic mean (confidence interval 90%)	0.51 (0.43 to 0.59)			

Statistical analyses

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 25 mg BID

Statistical analysis description:

The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the statistical analysis plan (SAP).

Comparison groups	DGAT2i/PF-06865571 25 mg BID v Placebo
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.08
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.02
upper limit	0.2

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 75 mg BID

Statistical analysis description:

The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.

Comparison groups	Placebo v DGAT2i/PF-06865571 75 mg BID
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.03
upper limit	0.24

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 150 mg BID

Statistical analysis description:

The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.

Comparison groups	Placebo v DGAT2i/PF-06865571 150 mg BID
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.12
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.03
upper limit	0.26

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 300 mg BID

Statistical analysis description:

The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.

Comparison groups	Placebo v DGAT2i/PF-06865571 300 mg BID
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.13
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.04
upper limit	0.28

Primary: Number of Participants Achieving Resolution of NASH Without Worsening or Improvement in Fibrosis by >= 1 Stage Without Worsening of NASH or Both Based on Assessment by Sponsor-Identified Central Pathologist at Week 48: Logistic Regression Model

End point title	Number of Participants Achieving Resolution of NASH Without Worsening or Improvement in Fibrosis by >= 1 Stage Without Worsening of NASH or Both Based on Assessment by Sponsor-Identified Central Pathologist at Week 48: Logistic Regression Model

End point description:

Resolution of NASH: disappearance of ballooning (NAS ballooning score = 0), residual or no lobular inflammation (NAS lobular inflammation score of 0 or 1) and NAS steatosis score of 0, 1, 2 or 3. No worsening of fibrosis: no change or a decrease of at least 1 stage in Brunt-Kleiner scale compared to baseline. Improvement of fibrosis by >= 1 stage: a decrease of at least 1 stage in Brunt-Kleiner scale compared to baseline. No worsening of NASH: no change or no increase in NAS for ballooning, inflammation, steatosis compared to baseline. Brunt-Kleiner scale indicated scaling for fibrosis. Full analysis set included all randomised participants who took at least 1 dose of investigational product who had provided baseline data for the primary endpoint. Participants were analysed according to the treatment group they were randomised to.

End point type	Primary

End point timeframe:

Week 48

End point values	Placebo	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID	DGAT2i/PF-06865571 150 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	35	48	42
Units: Participants	13	16	25	21

End point values	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID	DGAT2i/PF-06865571 300 mg BID	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	31	30	
Units: Participants	23	14	19	

Statistical analyses

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 25 mg BID

Statistical analysis description:

Logistic Regression model is used with treatment and baseline fibrosis stage (F2/F3) as factors. Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo rate and estimated odds ratio from the logistic regression model.

Comparison groups	Placebo v DGAT2i/PF-06865571 25 mg BID
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.08
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.11
upper limit	0.27

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 75 mg BID

Statistical analysis description:

Logistic Regression model is used with treatment and baseline fibrosis stage (F2/F3) as factors. Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo rate and estimated odds ratio from the logistic regression model.

Comparison groups	Placebo v DGAT2i/PF-06865571 75 mg BID
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.14
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.04
upper limit	0.32

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 150 mg BID

Statistical analysis description:

Logistic Regression model is used with treatment and baseline fibrosis stage (F2/F3) as factors. Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo rate and estimated odds ratio from the logistic regression model.

Comparison groups	Placebo v DGAT2i/PF-06865571 150 mg BID
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.12
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.07
upper limit	0.3

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 300 mg BID

Statistical analysis description:

Logistic Regression model is used with treatment and baseline fibrosis stage (F2/F3) as factors. Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo rate and estimated odds ratio from the logistic regression model.

Comparison groups	Placebo v DGAT2i/PF-06865571 300 mg BID
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.07
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.12
upper limit	0.27

Secondary: Percent Change From Baseline in Liver fat at Week 48: Bayesian Dose Response Model

End point title	Percent Change From Baseline in Liver fat at Week 48: Bayesian Dose Response Model[2]

End point description:

Magnetic resonance imaging proton density fat fraction (MRI-PDFF) is an established method that enables quantification of fat content in the liver. Bayesian dose response model was utilised to characterise the dose response across all BID treatment groups, to estimate the posterior mean relative change from baseline (and 90% credible interval) for each BID dose studied, and to estimate the placebo adjusted posterior mean relative change from baseline for each dose (and 90% credible interval). Full analysis set: all randomised participants who took at least 1 dose of investigational product who had provided baseline data for primary endpoint. Participants were analysed according to treatment group they were randomised to. This endpoint was not planned to be analysed in combination arms. Here, ''Number of Subjects Analysed'' signifies participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 48

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is reporting statistics for the arms specified

End point values	Placebo	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID	DGAT2i/PF-06865571 150 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	14	21	18
Units: Percent change				
arithmetic mean (confidence interval 90%)	-10.79 (-38.30 to 18.99)	-36.76 (-52.57 to -20.15)	-46.20 (-59.64 to -32.82)	-51.33 (-66.78 to -36.59)

End point values	DGAT2i/PF-06865571 300 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Percent change				
arithmetic mean (confidence interval 90%)	-55.53 (-77.23 to -37.64)			

Statistical analyses

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 25 mg BID
Statistical analysis description:	
The model utilised a Bayesian methodology approach with non-informative priors as described in the statistical analysis plan (SAP).	
Comparison groups	Placebo v DGAT2i/PF-06865571 25 mg BID
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Means
Point estimate	-25.98
Confidence interval	
level	90 %
sides	2-sided
lower limit	-58.42
upper limit	-2.57

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 75 mg BID
Statistical analysis description:	
The model utilised a Bayesian methodology approach with non-informative priors as described in the statistical analysis plan (SAP).	
Comparison groups	Placebo v DGAT2i/PF-06865571 75 mg BID
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Means
Point estimate	-35.41
Confidence interval	
level	90 %
sides	2-sided
lower limit	-69.41
upper limit	-5.42

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 150 mg BID
Statistical analysis description: The model utilised a Bayesian methodology approach with non-informative priors as described in the statistical analysis plan (SAP).	
Comparison groups	Placebo v DGAT2i/PF-06865571 150 mg BID
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Means
Point estimate	-40.54
Confidence interval	
level	90 %
sides	2-sided
lower limit	-75.55
upper limit	-7.32

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 300 mg BID
Statistical analysis description: The model utilised a Bayesian methodology approach with non-informative priors as described in the statistical analysis plan (SAP).	
Comparison groups	Placebo v DGAT2i/PF-06865571 300 mg BID
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Means
Point estimate	-44.74
Confidence interval	
level	90 %
sides	2-sided
lower limit	-81.72
upper limit	-8.42

Secondary: Percent Change From Baseline in Liver fat at Week 48: Pairwise Comparisons with Analysis of Covariance (ANCOVA)

End point title	Percent Change From Baseline in Liver fat at Week 48: Pairwise Comparisons with Analysis of Covariance (ANCOVA)
End point description: MRI-PDFF is an established method that enables quantification of fat content in the liver. Full analysis set included all randomised participants who took at least 1 dose of investigational product who had provided baseline data for primary endpoint. Participants were analysed according to treatment group they were randomised to. This endpoint was not planned to be analysed in combination arms. Here, ''Number of Subjects Analysed'' signifies participants evaluable for this endpoint.	
End point type	Secondary
End point timeframe: Baseline, Week 48	

End point values	Placebo	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID	DGAT2i/PF-06865571 150 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	12	18	12
Units: Percent change				
least squares mean (standard error)	1.41 (± 22.11)	-41.00 (± 18.89)	-42.53 (± 15.66)	-58.77 (± 19.44)

End point values	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID	DGAT2i/PF-06865571 300 mg BID	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	8	8	
Units: Percent change				
least squares mean (standard error)	-67.76 (± 19.93)	-49.76 (± 23.70)	-68.83 (± 23.72)	

Statistical analyses

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 25 mg BID

Statistical analysis description:

Log-transformed relative changes from baseline are modelled using an ANCOVA model with treatment and baseline fibrosis stage (F2/F3) as factors, and log-transformed baseline liver fat as a covariate.

Comparison groups	Placebo v DGAT2i/PF-06865571 25 mg BID
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean
Point estimate	-41.82
Confidence interval	
level	90 %
sides	2-sided
lower limit	-62.57
upper limit	-9.57

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 75 mg BID

Statistical analysis description:

Log-transformed relative changes from baseline are modelled using an ANCOVA model with treatment and baseline fibrosis stage (F2/F3) as factors, and log-transformed baseline liver fat as a covariate.

Comparison groups	Placebo v DGAT2i/PF-06865571 75 mg BID

Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean
Point estimate	-43.33
Confidence interval	
level	90 %
sides	2-sided
lower limit	-62.37
upper limit	-14.64

Statistical analysis title	Placebo vs DGAT2i 150 mg BID + ACCi 5 mg BID
Statistical analysis description:	
Log-transformed relative changes from baseline are modelled using an ANCOVA model with treatment and baseline fibrosis stage (F2/F3) as factors, and log-transformed baseline liver fat as a covariate.	
Comparison groups	Placebo v DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean
Point estimate	-68.21
Confidence interval	
level	90 %
sides	2-sided
lower limit	-79.72
upper limit	-50.15

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 150 mg BID
Statistical analysis description:	
Log-transformed relative changes from baseline are modelled using an ANCOVA model with treatment and baseline fibrosis stage (F2/F3) as factors, and log-transformed baseline liver fat as a covariate.	
Comparison groups	Placebo v DGAT2i/PF-06865571 150 mg BID
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean
Point estimate	-59.35
Confidence interval	
level	90 %
sides	2-sided
lower limit	-73.95
upper limit	-36.55

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 300 mg BID

Statistical analysis description:	
Log-transformed relative changes from baseline are modelled using an ANCOVA model with treatment and baseline fibrosis stage (F2/F3) as factors, and log-transformed baseline liver fat as a covariate.	
Comparison groups	Placebo v DGAT2i/PF-06865571 300 mg BID
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean
Point estimate	-50.46
Confidence interval	
level	90 %
sides	2-sided
lower limit	-69.53
upper limit	-19.44

Statistical analysis title	Placebo vs DGAT2i 300 mg BID + ACCi 10 mg BID
Statistical analysis description:	
Log-transformed relative changes from baseline are modelled using an ANCOVA model with treatment and baseline fibrosis stage (F2/F3) as factors, and log-transformed baseline liver fat as a covariate.	
Comparison groups	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID v Placebo
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean
Point estimate	-69.27
Confidence interval	
level	90 %
sides	2-sided
lower limit	-81.08
upper limit	-50.07

Statistical analysis title	DGAT2i 300mg BID vs DGAT2i 300mg BID+ACCi 10mg BID
Statistical analysis description:	
Log-transformed relative changes from baseline are modelled using an ANCOVA model with treatment and baseline fibrosis stage (F2/F3) as factors, and log-transformed baseline liver fat as a covariate.	
Comparison groups	DGAT2i/PF-06865571 300 mg BID v DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean
Point estimate	-37.97
Confidence interval	
level	90 %
sides	2-sided
lower limit	-62.41
upper limit	2.37

Statistical analysis title	DGAT2i 300mg BID vs DGAT2i 300mg BID+ACCi 10mg BID
Statistical analysis description: Log-transformed relative changes from baseline are modelled using an ANCOVA model with treatment and baseline fibrosis stage (F2/F3) as factors, and log-transformed baseline liver fat as a covariate.	
Comparison groups	DGAT2i/PF-06865571 300 mg BID v DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean
Point estimate	-37.97
Confidence interval	
level	Other: 50 %
sides	2-sided
lower limit	-49.4
upper limit	-23.95

Statistical analysis title	DGAT2i 150mg BID vs DGAT2i 150mg BID+ACCi 5mg BID
Statistical analysis description: Log-transformed relative changes from baseline are modelled using an ANCOVA model with treatment and baseline fibrosis stage (F2/F3) as factors, and log-transformed baseline liver fat as a covariate.	
Comparison groups	DGAT2i/PF-06865571 150 mg BID v DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean
Point estimate	-21.8
Confidence interval	
level	Other: 50 %
sides	2-sided
lower limit	-34.02
upper limit	-7.32

Statistical analysis title	DGAT2i 150mg BID vs DGAT2i 150mg BID+ACCi 5mg BID
Statistical analysis description: Log-transformed relative changes from baseline are modelled using an ANCOVA model with treatment and baseline fibrosis stage (F2/F3) as factors, and log-transformed baseline liver fat as a covariate.	
Comparison groups	DGAT2i/PF-06865571 150 mg BID v DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID

Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean
Point estimate	-21.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-48.51
upper limit	18.76

Secondary: Mean Proportion of Participants Achieving Resolution of NASH, Without Worsening of Fibrosis Based on Assessment by Sponsor-Identified Central Pathologist(s) at Week 48: Bayesian Dose Response Model

End point title	Mean Proportion of Participants Achieving Resolution of NASH, Without Worsening of Fibrosis Based on Assessment by Sponsor-Identified Central Pathologist(s) at Week 48: Bayesian Dose Response Model[3]

End point description:

Resolution of NASH: disappearance of ballooning (NAS ballooning score= 0), residual or no lobular inflammation (NAS lobular inflammation score of 0 or 1), NAS steatosis score of 0, 1, 2, 3. No worsening of fibrosis: no change/decrease of at least 1 stage in BKS compared to baseline. BKS: scaling for fibrosis. Bayesian dose response model was utilised to characterise dose response across all BID treatment groups, estimate posterior mean relative change from baseline (and 90% CI) for BID dose studied, estimate placebo adjusted posterior mean relative change from baseline for each dose (and 90% CI). c Full analysis set: all randomised participants who took at least 1 dose of investigational product who had provided baseline data for primary endpoint. Participants were analysed according to treatment group they were randomised to. Endpoint was not planned to be analysed in combination arms.

End point type	Secondary

End point timeframe:

Week 48

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is reporting statistics for the arms specified

End point values	Placebo	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID	DGAT2i/PF-06865571 150 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	35	48	42
Units: Proportion of participants				
arithmetic mean (confidence interval 90%)	0.11 (0.04 to 0.20)	0.32 (0.23 to 0.40)	0.37 (0.31 to 0.44)	0.40 (0.33 to 0.47)

End point values	DGAT2i/PF-06865571 300 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: Proportion of participants				

arithmetic mean (confidence interval 90%)	0.41 (0.34 to 0.50)			

Statistical analyses

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 25 mg BID

Statistical analysis description:

The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.

Comparison groups	Placebo v DGAT2i/PF-06865571 25 mg BID
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.21
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.09
upper limit	0.32

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 300 mg BID

Statistical analysis description:

The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.

Comparison groups	Placebo v DGAT2i/PF-06865571 300 mg BID
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.31
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.19
upper limit	0.42

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 150 mg BID

Statistical analysis description:

The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.

Comparison groups	Placebo v DGAT2i/PF-06865571 150 mg BID

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.29
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.18
upper limit	0.39

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 75 mg BID

Statistical analysis description:

The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.

Comparison groups	Placebo v DGAT2i/PF-06865571 75 mg BID
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.27
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.15
upper limit	0.37

Secondary: Number of Participants Achieving Resolution of NASH, Without Worsening of Fibrosis Based on Assessment by Sponsor-Identified Central Pathologist(s) at Week 48: Pairwise Comparisons With Logistic Regression Model

End point title	Number of Participants Achieving Resolution of NASH, Without Worsening of Fibrosis Based on Assessment by Sponsor-Identified Central Pathologist(s) at Week 48: Pairwise Comparisons With Logistic Regression Model

End point description:

Resolution of NASH: disappearance of ballooning (NAS ballooning score= 0), residual or no lobular inflammation (NAS lobular inflammation score of 0 or 1), NAS steatosis score of 0, 1, 2 or 3. No worsening of fibrosis: no change or decrease of at least 1 stage in Brunt-Kleiner scale compared to baseline. Brunt-Kleiner scale included scaling for fibrosis. Full analysis set included all randomised participants who took at least 1 dose of investigational product who had provided baseline data for primary endpoint. Participants were analysed according to treatment group they were randomised to.

End point type	Secondary

End point timeframe:

Week 48

End point values	Placebo	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID	DGAT2i/PF-06865571 150 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	35	48	42
Units: Participants	3	11	22	13

End point values	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID	DGAT2i/PF-06865571 300 mg BID	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	31	30	
Units: Participants	22	13	17	

Statistical analyses

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 25 mg BID

Statistical analysis description:

Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.

Comparison groups	Placebo v DGAT2i/PF-06865571 25 mg BID
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.23
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.04
upper limit	0.51

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 75 mg BID

Statistical analysis description:

Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.

Comparison groups	Placebo v DGAT2i/PF-06865571 75 mg BID
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.37

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.13
upper limit	0.63

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 150 mg BID

Statistical analysis description:

Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.

Comparison groups	Placebo v DGAT2i/PF-06865571 150 mg BID
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.22
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.04
upper limit	0.49

Statistical analysis title	Placebo vs DGAT2i 150 mg BID + ACCi 5 mg BID

Statistical analysis description:

Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.

Comparison groups	Placebo v DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.54
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.26
upper limit	0.75

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 300 mg BID

Statistical analysis description:

Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.

Comparison groups	Placebo v DGAT2i/PF-06865571 300 mg BID

Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.34
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.1
upper limit	0.61

Statistical analysis title	DGAT2i 150mg BID vs DGAT2i 150mg BID+ACCi 5mg BID
Statistical analysis description:	
Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	DGAT2i/PF-06865571 150 mg BID v DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.32
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.12
upper limit	0.48

Statistical analysis title	Placebo vs DGAT2i 300 mg BID + ACCi 10 mg BID
Statistical analysis description:	
Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	Placebo v DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.48
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.2
upper limit	0.72

Statistical analysis title	DGAT2i 150mg BID vs DGAT2i 150mg BID+ACCi 5mg BID
Statistical analysis description: Risk difference and 2-sided 50% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID v DGAT2i/PF-06865571 150 mg BID
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.32
Confidence interval	
level	Other: 50 %
sides	2-sided
lower limit	0.24
upper limit	0.39

Statistical analysis title	DGAT2i 300mg BID vs DGAT2i 300mg BID+ACCi 10mg BID
Statistical analysis description: Risk difference and 2-sided 50% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	DGAT2i/PF-06865571 300 mg BID v DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.14
Confidence interval	
level	Other: 50 %
sides	2-sided
lower limit	0.06
upper limit	0.23

Statistical analysis title	DGAT2i 300mg BID vs DGAT2i 300mg BID+ACCi 10mg BID
Statistical analysis description: Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	DGAT2i/PF-06865571 300 mg BID v DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.14

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.06
upper limit	0.33

Secondary: Mean Proportion of Participants Achieving Improvement in Fibrosis by >=1 Stage, Without Worsening of NASH Based on Assessment by Sponsor-Identified Central Pathologist(s) at Week 48: Bayesian Dose Response Model

End point title	Mean Proportion of Participants Achieving Improvement in Fibrosis by >=1 Stage, Without Worsening of NASH Based on Assessment by Sponsor-Identified Central Pathologist(s) at Week 48: Bayesian Dose Response Model[4]

End point description:

Improvement in fibrosis by >=1 stage: decrease of at least 1 stage in Brunt-Kleiner scale compared to baseline. No worsening of NASH: no change or no increase in NAS for ballooning, inflammation, or steatosis compared to baseline. Brunt-Kleiner scale included scaling for fibrosis. Bayesian dose response model was utilised to characterise the dose response across all BID treatment groups, to estimate the posterior mean relative change from baseline (and 90% credible interval) for each BID dose studied, and to estimate the placebo adjusted posterior mean relative change from baseline for each dose (and 90% credible interval). Full analysis set included all randomised participants who took at least 1 dose of investigational product who had provided baseline data for primary endpoint. Participants were analysed according to treatment group they were randomised to. This endpoint was not planned to be analysed in combination arms.

End point type	Secondary

End point timeframe:

Week 48

Notes:

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

End point values	Placebo	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID	DGAT2i/PF-06865571 150 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	35	48	42
Units: Proportion of participants				
arithmetic mean (confidence interval 90%)	0.33 (0.22 to 0.45)	0.28 (0.21 to 0.35)	0.25 (0.20 to 0.31)	0.24 (0.18 to 0.30)

End point values	DGAT2i/PF-06865571 300 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: Proportion of participants				
arithmetic mean (confidence interval 90%)	0.22 (0.14 to 0.30)			

Statistical analyses

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 25 mg BID

Statistical analysis description:

The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.

Comparison groups	Placebo v DGAT2i/PF-06865571 25 mg BID
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	-0.05
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.16
upper limit	0.02

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 300 mg BID

Statistical analysis description:

The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.

Comparison groups	Placebo v DGAT2i/PF-06865571 300 mg BID
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	-0.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.26
upper limit	0.05

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 150 mg BID

Statistical analysis description:

The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.

Comparison groups	Placebo v DGAT2i/PF-06865571 150 mg BID
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	-0.09

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.23
upper limit	0.04

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 75 mg BID

Statistical analysis description:

The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.

Comparison groups	Placebo v DGAT2i/PF-06865571 75 mg BID
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	-0.07
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.2
upper limit	0.03

Secondary: Number of Participants Achieving Improvement in Fibrosis by >=1 Stage, Without Worsening of NASH Based on Assessment by Sponsor-Identified Central Pathologist(s) at Week 48: Pairwise Comparisons with Logistic Regression Model

End point title	Number of Participants Achieving Improvement in Fibrosis by >=1 Stage, Without Worsening of NASH Based on Assessment by Sponsor-Identified Central Pathologist(s) at Week 48: Pairwise Comparisons with Logistic Regression Model

End point description:

Improvement in fibrosis by >=1 stage: decrease of at least 1 stage in Brunt-Kleiner scale compared to baseline. No worsening of NASH: no change or no increase in NAS for ballooning, inflammation, or steatosis compared to baseline. Brunt-Kleiner scale included scaling fibrosis. Full analysis set included all randomised participants who took at least 1 dose of investigational product who had provided baseline data for primary endpoint. Participants were analysed according to treatment group they were randomised to.

End point type	Secondary

End point timeframe:

Week 48

End point values	Placebo	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID	DGAT2i/PF-06865571 150 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	35	48	42
Units: Participants	12	10	10	14

End point values	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID	DGAT2i/PF-06865571 300 mg BID	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	31	30	
Units: Participants	13	4	12	

Statistical analyses

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 25 mg BID

Statistical analysis description:

Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.

Comparison groups	Placebo v DGAT2i/PF-06865571 25 mg BID
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	-0.07
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.21
upper limit	0.13

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 75 mg BID

Statistical analysis description:

Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.

Comparison groups	Placebo v DGAT2i/PF-06865571 75 mg BID
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	-0.14

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.25
upper limit	0.02

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 150 mg BID
Statistical analysis description:	
Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	Placebo v DGAT2i/PF-06865571 150 mg BID
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	-0.02
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.17
upper limit	0.17

Statistical analysis title	Placebo vs DGAT2i 150 mg BID + ACCi 5 mg BID
Statistical analysis description:	
Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	Placebo v DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.02
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.15
upper limit	0.22

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 300 mg BID
Statistical analysis description:	
Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	Placebo v DGAT2i/PF-06865571 300 mg BID

Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	-0.22
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.3
upper limit	-0.05

Statistical analysis title	DGAT2i 150mg BID vs DGAT2i 150mg BID+ACCi 5mg BID
Statistical analysis description:	
Risk difference and 2-sided 50% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID v DGAT2i/PF-06865571 150 mg BID
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.04
Confidence interval	
level	Other: 50 %
sides	2-sided
lower limit	-0.03
upper limit	0.12

Statistical analysis title	Placebo vs DGAT2i 300 mg BID + ACCi 10 mg BID
Statistical analysis description:	
Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	Placebo v DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.05
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.13
upper limit	0.26

Statistical analysis title	DGAT2i 300mg BID vs DGAT2i 300mg BID+ACCi 10mg BID
Statistical analysis description: Risk difference and 2-sided 50% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	DGAT2i/PF-06865571 300 mg BID v DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.27
Confidence interval	
level	Other: 50 %
sides	2-sided
lower limit	0.17
upper limit	0.38

Statistical analysis title	DGAT2i 150mg BID vs DGAT2i 150mg BID+ACCi 5mg BID
Statistical analysis description: Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	DGAT2i/PF-06865571 150 mg BID v DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.04
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.12
upper limit	0.23

Statistical analysis title	DGAT2i 300mg BID vs DGAT2i 300mg BID+ACCi 10mg BID
Statistical analysis description: Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	DGAT2i/PF-06865571 300 mg BID v DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.27

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.06
upper limit	0.53

Secondary: Mean Proportion of Participants Achieving Improvement in Fibrosis by >=2 Stage, Without Worsening of NASH Based on Assessment by Sponsor-Identified Central Pathologist(s) at Week 48: Bayesian Dose Response Model

End point title	Mean Proportion of Participants Achieving Improvement in Fibrosis by >=2 Stage, Without Worsening of NASH Based on Assessment by Sponsor-Identified Central Pathologist(s) at Week 48: Bayesian Dose Response Model[5]

End point description:

Improvement in fibrosis by >=2 stage: decrease of at least 2 stages in the Brunt-Kleiner scale compared to baseline, without progression of fibrosis. No worsening of NASH: no change or no increase in NAS for ballooning, inflammation, or steatosis compared to baseline. Brunt-Kleiner scale included scaling for fibrosis. Bayesian dose response model was utilised to characterise the dose response across all BID treatment groups, to estimate the posterior mean proportion of responders (and 90% credible interval) for each BID dose studied. Full analysis set included all randomised participants who took at least 1 dose of investigational product who had provided baseline data for primary endpoint. Participants were analysed according to treatment group they were randomised to. This endpoint was not planned to be analysed in combination arms.

End point type	Secondary

End point timeframe:

Week 48

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is reporting statistics for the arms specified

End point values	Placebo	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID	DGAT2i/PF-06865571 150 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	35	48	42
Units: Proportion of participants				
arithmetic mean (confidence interval 90%)	0.05 (0.01 to 0.10)	0.08 (0.04 to 0.11)	0.09 (0.05 to 0.12)	0.09 (0.06 to 0.14)

End point values	DGAT2i/PF-06865571 300 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: Proportion of participants				
arithmetic mean (confidence interval 90%)	0.10 (0.06 to 0.16)			

Statistical analyses

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 25 mg BID

Statistical analysis description:

The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.

Comparison groups	Placebo v DGAT2i/PF-06865571 25 mg BID
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.03
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.01
upper limit	0.08

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 300 mg BID

Statistical analysis description:

The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.

Comparison groups	Placebo v DGAT2i/PF-06865571 300 mg BID
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.05
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.02
upper limit	0.12

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 150 mg BID

Statistical analysis description:

The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.

Comparison groups	Placebo v DGAT2i/PF-06865571 150 mg BID
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.05

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.02
upper limit	0.11

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 75 mg BID

Statistical analysis description:

The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.

Comparison groups	Placebo v DGAT2i/PF-06865571 75 mg BID
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.04
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.02
upper limit	0.09

Secondary: Number of Participants Achieving Improvement in Fibrosis by >=2 Stage, Without Worsening of NASH Based on Assessment by Sponsor-Identified Central Pathologist(s) at Week 48: Pairwise Comparisons with Logistic Regression Model

End point title	Number of Participants Achieving Improvement in Fibrosis by >=2 Stage, Without Worsening of NASH Based on Assessment by Sponsor-Identified Central Pathologist(s) at Week 48: Pairwise Comparisons with Logistic Regression Model

End point description:

Improvement in fibrosis by >=2 stage: decrease of at least 2 stages in the Brunt-Kleiner scale compared to baseline, without progression of fibrosis. No worsening of NASH: no change or no increase in NAS for ballooning, inflammation, or steatosis compared to baseline. Brunt-Kleiner scale included scaling for fibrosis. Full analysis set included all randomised participants who took at least 1 dose of investigational product who had provided baseline data for primary endpoint. Participants were analysed according to treatment group they were randomised to.

End point type	Secondary

End point timeframe:

Week 48

End point values	Placebo	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID	DGAT2i/PF-06865571 150 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	35	48	42
Units: Participants	1	4	3	5

End point values	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID	DGAT2i/PF-06865571 300 mg BID	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	31	30	
Units: Participants	7	2	6	

Statistical analyses

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 25 mg BID

Statistical analysis description:

Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.

Comparison groups	Placebo v DGAT2i/PF-06865571 25 mg BID
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.09
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.01
upper limit	0.43

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 75 mg BID

Statistical analysis description:

Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.

Comparison groups	Placebo v DGAT2i/PF-06865571 75 mg BID
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.03

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.02
upper limit	0.29

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 150 mg BID
Statistical analysis description:	
Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	Placebo v DGAT2i/PF-06865571 150 mg BID
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.09
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.01
upper limit	0.43

Statistical analysis title	Placebo vs DGAT2i 150 mg BID + ACCi 5 mg BID
Statistical analysis description:	
Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	Placebo v DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.17
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.01
upper limit	0.57

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 300 mg BID
Statistical analysis description:	
Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	Placebo v DGAT2i/PF-06865571 300 mg BID

Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.04
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.02
upper limit	0.33

Statistical analysis title	DGAT2i 150mg BID vs DGAT2i 150mg BID+ACCi 5mg BID
Statistical analysis description:	
Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	DGAT2i/PF-06865571 150 mg BID v DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.08
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.04
upper limit	0.3

Statistical analysis title	Placebo vs DGAT2i 300 mg BID + ACCi 10 mg BID
Statistical analysis description:	
Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	Placebo v DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.17
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.01
upper limit	0.58

Statistical analysis title	DGAT2i 150mg BID vs DGAT2i 150mg BID+ACCi 5mg BID
Statistical analysis description: Risk difference and 2-sided 50% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	DGAT2i/PF-06865571 150 mg BID v DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.08
Confidence interval	
level	Other: 50 %
sides	2-sided
lower limit	0.02
upper limit	0.16

Statistical analysis title	DGAT2i 300mg BID vs DGAT2i 300mg BID+ACCi 10mg BID
Statistical analysis description: Risk difference and 2-sided 50% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	DGAT2i/PF-06865571 300 mg BID v DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.13
Confidence interval	
level	Other: 50 %
sides	2-sided
lower limit	0.06
upper limit	0.24

Statistical analysis title	DGAT2i 300mg BID vs DGAT2i 300mg BID+ACCi 10mg BID
Statistical analysis description: Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	DGAT2i/PF-06865571 300 mg BID v DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.13

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.01
upper limit	0.44

Secondary: Mean Proportion of Participants Achieving Improvement of >=2 Points in Total NAS, Without Progression of Fibrosis Based on Assessment by Sponsor-Identified Central Pathologist(s) at Week 48: Bayesian Dose Response Model

End point title	Mean Proportion of Participants Achieving Improvement of >=2 Points in Total NAS, Without Progression of Fibrosis Based on Assessment by Sponsor-Identified Central Pathologist(s) at Week 48: Bayesian Dose Response Model[6]

End point description:

Improvement of >=2 points in Total NAS: decrease of at least 2 points in Total NAS compared to baseline, without progression of fibrosis. No progression of fibrosis: no change/decrease of at least 1 stage in BKS CTB. Total NAS ranged from 0 to 8, was calculated as sum of scores of steatosis (0 to 3), lobular inflammation (0 to 3), ballooning (0 to 2). BKS included scaling for fibrosis. If any of sub-scale scores were non evaluable/missing, total score was derived as missing. BDRM was utilised to characterise dose response across all BID treatment groups, estimate posterior mean relative change from baseline (90% CI) for each BID dose studied, estimate placebo adjusted posterior mean relative change from baseline for each dose (90% CI). CI=credible interval and note that CI labelled as confidence intervals below. Full analysis set was analysed. Participants were analysed according to treatment group they were randomised to. Endpoint was not planned to be analysed in combination arms.

End point type	Secondary

End point timeframe:

Week 48

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is reporting statistics for the arms specified

End point values	Placebo	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID	DGAT2i/PF-06865571 150 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	35	48	42
Units: Proportion of participants				
arithmetic mean (confidence interval 90%)	0.24 (0.13 to 0.37)	0.42 (0.33 to 0.50)	0.47 (0.40 to 0.54)	0.49 (0.42 to 0.57)

End point values	DGAT2i/PF-06865571 300 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: Proportion of participants				
arithmetic mean (confidence interval 90%)	0.51 (0.43 to 0.59)			

Statistical analyses

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 25 mg BID
Statistical analysis description:	
The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.	
Comparison groups	Placebo v DGAT2i/PF-06865571 25 mg BID
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.18
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.05
upper limit	0.31

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 150 mg BID
Statistical analysis description:	
The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.	
Comparison groups	Placebo v DGAT2i/PF-06865571 150 mg BID
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.25
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.1
upper limit	0.38

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 300 mg BID
Statistical analysis description:	
The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.	
Comparison groups	Placebo v DGAT2i/PF-06865571 300 mg BID

Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.27
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.11
upper limit	0.4

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 75 mg BID

Statistical analysis description:

The model was applied to the raw number of responders and non-responders utilising a Bayesian methodology approach with non-informative priors as described in the SAP.

Comparison groups	Placebo v DGAT2i/PF-06865571 75 mg BID
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.23
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.09
upper limit	0.36

Secondary: Number of Participants Achieving Improvement of >=2 Points in Total NAS Without Progression of Fibrosis Based on Assessment by Sponsor-Identified Central Pathologist(s) at Week 48: Pairwise Comparisons with Logistic Regression Model

End point title	Number of Participants Achieving Improvement of >=2 Points in Total NAS Without Progression of Fibrosis Based on Assessment by Sponsor-Identified Central Pathologist(s) at Week 48: Pairwise Comparisons with Logistic Regression Model

End point description:

Improvement of >=2 points in Total NAS was defined as a decrease of at least 2 points in Total NAS compared to baseline, without progression of fibrosis. No progression of fibrosis: no change or a decrease of at least 1 stage in the Brunt-Kleiner scale compared to baseline. Total NAS ranged from 0 to 8 and was calculated as the sum of scores of steatosis (0 to 3), lobular inflammation (0 to 3) and ballooning (0 to 2). Brunt-Kleiner scale included scaling for fibrosis. If any of the sub-scale scores were non evaluable/missing, then the total score was derived as missing. Full analysis set included all randomised participants who took at least 1 dose of investigational product who had provided baseline data for primary endpoint. Participants were analysed according to treatment group they were randomised to.

End point type	Secondary

End point timeframe:

Week 48

End point values	Placebo	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID	DGAT2i/PF-06865571 150 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	35	48	42
Units: Participants	8	13	28	21

End point values	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID	DGAT2i/PF-06865571 300 mg BID	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	31	30	
Units: Participants	25	12	19	

Statistical analyses

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 75 mg BID

Statistical analysis description:

Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.

Comparison groups	Placebo v DGAT2i/PF-06865571 75 mg BID
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.35
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.15
upper limit	0.53

Statistical analysis title	Placebo vs DGAT2i 150 mg BID + ACCi 5 mg BID

Statistical analysis description:

Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.

Comparison groups	Placebo v DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID

Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.48
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.27
upper limit	0.63

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 150 mg BID

Statistical analysis description:

Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.

Comparison groups	Placebo v DGAT2i/PF-06865571 150 mg BID
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.26
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.06
upper limit	0.46

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 25 mg BID

Statistical analysis description:

Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.

Comparison groups	Placebo v DGAT2i/PF-06865571 25 mg BID
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.14
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.04
upper limit	0.36

Statistical analysis title	DGAT2i 300mg BID vs DGAT2i 300mg BID+ACCi 10mg BID

Statistical analysis description:

Risk difference and 2-sided 50% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.

Comparison groups	DGAT2i/PF-06865571 300 mg BID v DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.24
Confidence interval	
level	Other: 50 %
sides	2-sided
lower limit	0.16
upper limit	0.32

Statistical analysis title	DGAT2i 150mg BID vs DGAT2i 150mg BID+ACCi 5mg BID

Statistical analysis description:

Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.

Comparison groups	DGAT2i/PF-06865571 150 mg BID v DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.22
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.03
upper limit	0.35

Statistical analysis title	DGAT2i 150mg BID vs DGAT2i 150mg BID+ACCi 5mg BID

Statistical analysis description:

Risk difference and 2-sided 50% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.

Comparison groups	DGAT2i/PF-06865571 150 mg BID v DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.22

Confidence interval	
level	Other: 50 %
sides	2-sided
lower limit	0.15
upper limit	0.28

Statistical analysis title	Placebo vs DGAT2i/PF-06865571 300 mg BID
Statistical analysis description:	
Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	Placebo v DGAT2i/PF-06865571 300 mg BID
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.16
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.03
upper limit	0.38

Statistical analysis title	Placebo vs DGAT2i 300 mg BID + ACCi 10 mg BID
Statistical analysis description:	
Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	Placebo v DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.18
upper limit	0.58

Statistical analysis title	DGAT2i 300mg BID vs DGAT2i 300mg BID+ACCi 10mg BID
Statistical analysis description:	
Risk difference and 2-sided 90% confidence interval for risk difference were calculated by using the observed placebo/corresponding BID rate and estimated odds ratio from the logistic regression model.	
Comparison groups	DGAT2i/PF-06865571 300 mg BID v DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID

Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	0.24
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.03
upper limit	0.42

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

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

End point description:

An adverse event (AE) was any untoward medical occurrence in a participant/ clinical investigational participant administered a medicinal product and which does not necessarily have a causal relationship with this treatment. Serious adverse events (SAE) was any untoward medical occurrence at any dose that: resulted in death, was life threatening (risk of death), required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions), resulted in congenital anomaly/birth defect. AEs included both serious and all non-serious AEs. TEAEs were defined as newly occurring or worsening AE after the first dose of study drug. Safety population included all participants who took at least 1 dose of investigational product. Participants were analysed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

From first dose of study drug (Day 1) up to Week 48 (maximum up to approximately 52 weeks)

End point values	Placebo	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID	DGAT2i/PF-06865571 150 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	35	48	42
Units: Participants	26	25	38	30

End point values	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID	DGAT2i/PF-06865571 300 mg BID	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	31	30	
Units: Participants	25	26	23	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Laboratory Test Abnormalities

End point title	Number of Participants With Laboratory Test Abnormalities

End point description:

Hematology(Hemoglobin [hgb],hematocrit,erythrocytes [ery]:<0.8*lower limit of normal [LLN];reticulocytes,reticulocytes/ery:<0.5*LLN, >1.5*upper LN [ULN];ery mean corpuscular volume [EMC],EMC hgb: <0.9*LLN, >1.1*ULN;platelet:>1.75 ULN; lymphocytes,neutrophils,basophils, eosinophils: <0.8* LLN, >1.2*ULN;monocytes: >1.2*ULN;activated partial thromboplastin time,prothrombin time: >1.1*ULN);Clinical chemistry (Total/direct bilirubin,glucose:>1.5*ULN;aspartate aminotransferase [AT], alanine AT,gamma glutamyl transferase: >3.0*ULN;HDL cholesterol: <0.8*LLN;urea nitrogen,creatinine,triglyceride,cholesterol,hgb A1C: >1.3*ULN;urate: >1.2*ULN;potassium: <0.9*LLN, >1.1*ULN;sodium: <0.95*LLN;calcium,bicarbonate: <0.9*LLN;creatine kinase: >2.0*ULN); Urinalysis (glucose,protein,hgb,ketones,nitrite,leukocyte esterase, urobilinogen,bilirubin: >=1; ery,leukocytes: >=20;granular,hyaline casts: >1). Safety population was analysed. ''Number of Subjects Analysed''=participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From first dose of study drug (Day 1) up to Week 48 (maximum up to approximately 52 weeks)

End point values	Placebo	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID	DGAT2i/PF-06865571 150 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	34	48	42
Units: Participants	31	32	46	39

End point values	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID	DGAT2i/PF-06865571 300 mg BID	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	31	30	
Units: Participants	34	27	30	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Abnormalities in Vital Signs

End point title	Number of Participants With Clinically Significant Abnormalities in Vital Signs

End point description:

Number of participants with clinically significant laboratory abnormalities were reported in this endpoint. Vital signs included blood pressure, and heart rate. Clinical significance in vital signs abnormalities was judged by investigator. Safety population included all participants who took at least 1 dose of investigational product. Participants were analysed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

From first dose of study drug (Day 1) up to Week 48 (maximum up to approximately 50 weeks)

End point values	Placebo	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID	DGAT2i/PF-06865571 150 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	35	48	42
Units: Participants	0	0	0	0

End point values	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID	DGAT2i/PF-06865571 300 mg BID	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	31	30	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Abnormalities in Electrocardiograms (ECG) Parameters

End point title	Number of Participants With Clinically Significant Abnormalities in Electrocardiograms (ECG) Parameters

End point description:

Number of participants with clinically significant ECG abnormalities were reported in this outcome measure. ECG parameters included heart rate, PR, QRS and QTcF interval. Safety population included all participants who took at least 1 dose of investigational product. Participants were analysed according to the treatment they actually received. Here, ''Number of Subjects Analysed'' signifies participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From first dose of study drug (Day 1) up to Week 48 (maximum up to approximately 50 weeks)

End point values	Placebo	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID	DGAT2i/PF-06865571 150 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	32	47	39
Units: Participants	0	0	0	0

End point values	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID	DGAT2i/PF-06865571 300 mg BID	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	28	28	
Units: Participants	0	0	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 drug (Day 1) up to 4 weeks after last dose of study drug (maximum up to approximately 52 weeks)

Adverse event reporting additional description:

Same event may appear as both non-SAE and SAE but what is presented are distinct events. Event may be categorized as serious in 1 participant and non-serious in other, or participant may have experienced both serious and non-serious event. Safety population included all participants who took at least 1 dose of investigational product.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants were randomized to receive 2 tablets of DGAT2i matching placebo and 1 tablet of ACCi matching placebo BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.

Reporting group title	DGAT2i/PF-06865571 150 mg BID

Reporting group description:

Participants were randomized to receive 1 tablet of DGAT2i matching placebo, 1 tablet of DGAT2i 150 mg and 1 tablet of ACCi matching placebo BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.

Reporting group title	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID

Reporting group description:

Participants were randomized to receive 1 tablet of DGAT2i matching placebo, 1 tablet of DGAT2i 150 mg and 1 tablet of ACCi 5 mg BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.

Reporting group title	DGAT2i/PF-06865571 25 mg BID

Reporting group description:

Participants were randomized to receive 1 tablet of DGAT2i 25 mg along with 1 tablet of DGAT2i and ACCi matching placebo BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.

Reporting group title	DGAT2i/PF-06865571 75 mg BID

Reporting group description:

Participants were randomized to receive 1 tablet of DGAT2i 25 mg, 1 tablet of DGAT2i 50 mg and 1 tablet of ACCi matching placebo BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.

Reporting group title	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID

Reporting group description:

Participants were randomized to receive 2 tablets of DGAT2i 150 mg and 1 tablet of ACCi 10 mg BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.

Reporting group title	DGAT2i/PF-06865571 300 mg BID

Reporting group description:

Participants were randomized to receive 2 tablets of DGAT2i 150 mg and 1 tablet of ACCi matching placebo BID for 48 weeks by oral administration. Participants were followed up to 52 weeks.

Serious adverse events	Placebo	DGAT2i/PF-06865571 150 mg BID	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 34 (2.94%)	1 / 42 (2.38%)	5 / 35 (14.29%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	0 / 35 (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
Mucoepidermoid carcinoma			
subjects affected / exposed	0 / 34 (0.00%)	1 / 42 (2.38%)	0 / 35 (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
Vascular disorders			
Venous thrombosis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	0 / 35 (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
Cardiac disorders			
Coronary artery stenosis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	0 / 35 (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 infarction			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	0 / 35 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	0 / 35 (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
Gastrointestinal disorders			

Constipation			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	0 / 35 (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
Obstructive pancreatitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	0 / 35 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	0 / 35 (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			
Cholecystitis acute			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	0 / 35 (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
Hepatic haemorrhage			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcapsular hepatic haematoma			

subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	0 / 35 (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
Drug-induced liver injury			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	0 / 35 (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			
Acute kidney injury			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	0 / 35 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	1 / 35 (2.86%)
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 / 34 (2.94%)	0 / 42 (0.00%)	0 / 35 (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
COVID-19			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	0 / 35 (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

Serious adverse events	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID
Total subjects affected by serious			

adverse events			
subjects affected / exposed	1 / 35 (2.86%)	5 / 48 (10.42%)	2 / 30 (6.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 35 (0.00%)	1 / 48 (2.08%)	0 / 30 (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
Mucoepidermoid carcinoma			
subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	0 / 30 (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
Vascular disorders			
Venous thrombosis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 48 (2.08%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Cardiac disorders			
Coronary artery stenosis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 35 (0.00%)	1 / 48 (2.08%)	0 / 30 (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			
Constipation			

subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	0 / 30 (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
Obstructive pancreatitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	0 / 30 (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
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	0 / 30 (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			
Asthma			
subjects affected / exposed	0 / 35 (0.00%)	1 / 48 (2.08%)	0 / 30 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 35 (0.00%)	1 / 48 (2.08%)	0 / 30 (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
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 35 (0.00%)	1 / 48 (2.08%)	0 / 30 (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
Hepatic haemorrhage			
subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	0 / 30 (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
Subcapsular hepatic haematoma			

subjects affected / exposed	0 / 35 (0.00%)	1 / 48 (2.08%)	0 / 30 (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
Drug-induced liver injury			
subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	0 / 30 (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			
Acute kidney injury			
subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	0 / 30 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	0 / 30 (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
Osteoarthritis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	0 / 30 (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			
Appendicitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	0 / 30 (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
COVID-19			
subjects affected / exposed	1 / 35 (2.86%)	0 / 48 (0.00%)	0 / 30 (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	DGAT2i/PF-06865571 300 mg BID		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 31 (12.90%)		

number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mucoepidermoid carcinoma			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Venous thrombosis			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Coronary artery stenosis			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Obstructive pancreatitis				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Benign prostatic hyperplasia				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Asthma				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis acute				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatic haemorrhage				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subcapsular hepatic haematoma				
subjects affected / exposed	0 / 31 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug-induced liver injury				

subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	DGAT2i/PF-06865571 150 mg BID	DGAT2i/PF-06865571 150 mg BID + ACCi/PF-05221304 5 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 34 (61.76%)	22 / 42 (52.38%)	19 / 35 (54.29%)

Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 34 (0.00%)	2 / 42 (4.76%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Alanine aminotransferase increased			
subjects affected / exposed	2 / 34 (5.88%)	0 / 42 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 34 (0.00%)	1 / 42 (2.38%)	2 / 35 (5.71%)
occurrences (all)	0	1	2
Procedural pain			
subjects affected / exposed	0 / 34 (0.00%)	1 / 42 (2.38%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 34 (0.00%)	1 / 42 (2.38%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	4 / 34 (11.76%)	1 / 42 (2.38%)	4 / 35 (11.43%)
occurrences (all)	4	1	4
Hypoaesthesia			
subjects affected / exposed	2 / 34 (5.88%)	0 / 42 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 34 (0.00%)	1 / 42 (2.38%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Puncture site pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	2 / 34 (5.88%)	1 / 42 (2.38%)	1 / 35 (2.86%)
occurrences (all)	4	1	1
Gastrointestinal disorders			

Abdominal pain upper			
subjects affected / exposed	3 / 34 (8.82%)	3 / 42 (7.14%)	2 / 35 (5.71%)
occurrences (all)	4	3	2
Abdominal pain			
subjects affected / exposed	1 / 34 (2.94%)	2 / 42 (4.76%)	1 / 35 (2.86%)
occurrences (all)	1	2	1
Vomiting			
subjects affected / exposed	0 / 34 (0.00%)	2 / 42 (4.76%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Diarrhoea			
subjects affected / exposed	2 / 34 (5.88%)	1 / 42 (2.38%)	2 / 35 (5.71%)
occurrences (all)	2	1	2
Constipation			
subjects affected / exposed	0 / 34 (0.00%)	3 / 42 (7.14%)	2 / 35 (5.71%)
occurrences (all)	0	3	2
Reproductive system and breast disorders			
Postmenopausal haemorrhage			
subjects affected / exposed	1 / 34 (2.94%)	0 / 42 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 34 (5.88%)	1 / 42 (2.38%)	1 / 35 (2.86%)
occurrences (all)	2	1	2
Nasal congestion			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Oropharyngeal pain			
subjects affected / exposed	0 / 34 (0.00%)	2 / 42 (4.76%)	1 / 35 (2.86%)
occurrences (all)	0	2	1
Skin and subcutaneous tissue disorders			
Asteatosis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	0 / 34 (0.00%)	2 / 42 (4.76%)	1 / 35 (2.86%)
occurrences (all)	0	2	1
Arthralgia			
subjects affected / exposed	2 / 34 (5.88%)	2 / 42 (4.76%)	3 / 35 (8.57%)
occurrences (all)	2	3	3
Osteoarthritis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 42 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	1 / 34 (2.94%)	3 / 42 (7.14%)	3 / 35 (8.57%)
occurrences (all)	1	4	5
Muscle spasms			
subjects affected / exposed	0 / 34 (0.00%)	1 / 42 (2.38%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 34 (2.94%)	1 / 42 (2.38%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
COVID-19			
subjects affected / exposed	2 / 34 (5.88%)	3 / 42 (7.14%)	1 / 35 (2.86%)
occurrences (all)	2	3	1
Nasopharyngitis			
subjects affected / exposed	4 / 34 (11.76%)	2 / 42 (4.76%)	2 / 35 (5.71%)
occurrences (all)	5	3	2
Upper respiratory tract infection			
subjects affected / exposed	1 / 34 (2.94%)	0 / 42 (0.00%)	4 / 35 (11.43%)
occurrences (all)	1	0	5
Tooth abscess			
subjects affected / exposed	0 / 34 (0.00%)	0 / 42 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Sinusitis			
subjects affected / exposed	0 / 34 (0.00%)	4 / 42 (9.52%)	3 / 35 (8.57%)
occurrences (all)	0	5	4
Urinary tract infection			

subjects affected / exposed	1 / 34 (2.94%)	3 / 42 (7.14%)	2 / 35 (5.71%)
occurrences (all)	1	3	2
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	4 / 34 (11.76%)	3 / 42 (7.14%)	2 / 35 (5.71%)
occurrences (all)	4	4	2

Non-serious adverse events	DGAT2i/PF-06865571 25 mg BID	DGAT2i/PF-06865571 75 mg BID	DGAT2i/PF-06865571 300 mg BID + ACCi/PF-05221304 10 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 35 (60.00%)	28 / 48 (58.33%)	15 / 30 (50.00%)
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 35 (2.86%)	1 / 48 (2.08%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 35 (2.86%)	0 / 48 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Procedural pain			
subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	4 / 30 (13.33%)
occurrences (all)	0	0	4
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 35 (0.00%)	2 / 48 (4.17%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Headache			
subjects affected / exposed	2 / 35 (5.71%)	5 / 48 (10.42%)	1 / 30 (3.33%)
occurrences (all)	2	6	1
Hypoaesthesia			
subjects affected / exposed	1 / 35 (2.86%)	0 / 48 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	0 / 35 (0.00%)	4 / 48 (8.33%)	1 / 30 (3.33%)
occurrences (all)	0	4	1
Puncture site pain			
subjects affected / exposed	2 / 35 (5.71%)	1 / 48 (2.08%)	0 / 30 (0.00%)
occurrences (all)	2	1	0
Pyrexia			
subjects affected / exposed	1 / 35 (2.86%)	3 / 48 (6.25%)	1 / 30 (3.33%)
occurrences (all)	2	4	2
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	4 / 35 (11.43%)	3 / 48 (6.25%)	0 / 30 (0.00%)
occurrences (all)	4	3	0
Vomiting			
subjects affected / exposed	1 / 35 (2.86%)	4 / 48 (8.33%)	2 / 30 (6.67%)
occurrences (all)	2	5	2
Diarrhoea			
subjects affected / exposed	1 / 35 (2.86%)	5 / 48 (10.42%)	2 / 30 (6.67%)
occurrences (all)	2	7	2
Constipation			
subjects affected / exposed	2 / 35 (5.71%)	1 / 48 (2.08%)	0 / 30 (0.00%)
occurrences (all)	2	1	0
Reproductive system and breast disorders			
Postmenopausal haemorrhage			
subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 35 (2.86%)	3 / 48 (6.25%)	0 / 30 (0.00%)
occurrences (all)	1	3	0
Nasal congestion			
subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0

Oropharyngeal pain			
subjects affected / exposed	1 / 35 (2.86%)	0 / 48 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Asteatosis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 35 (0.00%)	1 / 48 (2.08%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Arthralgia			
subjects affected / exposed	0 / 35 (0.00%)	2 / 48 (4.17%)	2 / 30 (6.67%)
occurrences (all)	0	2	3
Osteoarthritis			
subjects affected / exposed	2 / 35 (5.71%)	0 / 48 (0.00%)	1 / 30 (3.33%)
occurrences (all)	2	0	1
Pain in extremity			
subjects affected / exposed	0 / 35 (0.00%)	2 / 48 (4.17%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Muscle spasms			
subjects affected / exposed	0 / 35 (0.00%)	1 / 48 (2.08%)	2 / 30 (6.67%)
occurrences (all)	0	1	2
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 48 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	2 / 35 (5.71%)	4 / 48 (8.33%)	2 / 30 (6.67%)
occurrences (all)	2	4	2
Nasopharyngitis			
subjects affected / exposed	1 / 35 (2.86%)	4 / 48 (8.33%)	0 / 30 (0.00%)
occurrences (all)	11	5	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 35 (2.86%)	2 / 48 (4.17%)	2 / 30 (6.67%)
occurrences (all)	1	2	2

Tooth abscess			
subjects affected / exposed	1 / 35 (2.86%)	0 / 48 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Sinusitis			
subjects affected / exposed	2 / 35 (5.71%)	1 / 48 (2.08%)	0 / 30 (0.00%)
occurrences (all)	3	1	0
Urinary tract infection			
subjects affected / exposed	1 / 35 (2.86%)	0 / 48 (0.00%)	2 / 30 (6.67%)
occurrences (all)	1	0	2
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	6 / 35 (17.14%)	5 / 48 (10.42%)	2 / 30 (6.67%)
occurrences (all)	6	5	2

Non-serious adverse events	DGAT2i/PF-06865571 300 mg BID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 31 (61.29%)		
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	3		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	2		
Headache			

subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	3		
Puncture site pain			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	3		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Postmenopausal haemorrhage			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal			

disorders			
Cough			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Asteatosis			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	3		
Arthralgia			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	3		
Osteoarthritis			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
COVID-19			

subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	3		
Nasopharyngitis			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Tooth abscess			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 August 2021	Evaluation of 2 arms with administration of DGAT2i alone (150 mg once a day [QD] and 300 mg QD) was no longer being pursued. Those previously randomised to these 2 arms were switched in a blinded manner to receive the corresponding BID regimen that maintained the same total daily dose. Number randomised to trigger 1st safety review by E-DMC retained but proportion updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported