



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 (\geq) 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 (gestational 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 standard deviation | 55.21 ± 12.00 | 56.54 ± 11.38 | 56.02 ± 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 standard deviation | 55.95 ± 11.32 | 56.60 ± 10.23 | 59.65 ± 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 (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days - 23 months) | 0 | 0 | |
| Children (2 - 11 years) | 0 | 0 | |
| 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;creatinine 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 occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 31 (0.00%) 0 / 0 0 / 0 | | |
| Reproductive system and breast disorders Benign prostatic hyperplasia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 31 (0.00%) 0 / 0 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 31 (0.00%) 0 / 0 0 / 0 | | |
| Chronic obstructive pulmonary disease subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 31 (0.00%) 0 / 0 0 / 0 | | |
| Hepatobiliary disorders Cholecystitis acute subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 31 (3.23%) 0 / 1 0 / 0 | | |
| Hepatic haemorrhage subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 31 (3.23%) 0 / 1 0 / 0 | | |
| Subcapsular hepatic haematoma subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 31 (0.00%) 0 / 0 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 occurrences (all) | 3 / 34 (8.82%) 4 | 3 / 42 (7.14%) 3 | 2 / 35 (5.71%) 2 |
| Abdominal pain subjects affected / exposed occurrences (all) | 1 / 34 (2.94%) 1 | 2 / 42 (4.76%) 2 | 1 / 35 (2.86%) 1 |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 2 / 42 (4.76%) 2 | 0 / 35 (0.00%) 0 |
| Diarrhoea subjects affected / exposed occurrences (all) | 2 / 34 (5.88%) 2 | 1 / 42 (2.38%) 1 | 2 / 35 (5.71%) 2 |
| Constipation subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 3 / 42 (7.14%) 3 | 2 / 35 (5.71%) 2 |
| Reproductive system and breast disorders Postmenopausal haemorrhage subjects affected / exposed occurrences (all) | 1 / 34 (2.94%) 1 | 0 / 42 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 2 / 34 (5.88%) 2 | 1 / 42 (2.38%) 1 | 1 / 35 (2.86%) 2 |
| Nasal congestion subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 42 (0.00%) 0 | 2 / 35 (5.71%) 2 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 2 / 42 (4.76%) 2 | 1 / 35 (2.86%) 1 |
| Skin and subcutaneous tissue disorders Asteatosis subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 42 (0.00%) 0 | 2 / 35 (5.71%) 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 occurrences (all) | 1 / 34 (2.94%) 1 | 3 / 42 (7.14%) 3 | 2 / 35 (5.71%) 2 |
| Metabolism and nutrition disorders Diabetes mellitus inadequate control subjects affected / exposed occurrences (all) | 4 / 34 (11.76%) 4 | 3 / 42 (7.14%) 4 | 2 / 35 (5.71%) 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 occurrences (all) Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 35 (2.86%) 1 0 / 35 (0.00%) 0 | 1 / 48 (2.08%) 1 0 / 48 (0.00%) 0 | 0 / 30 (0.00%) 0 0 / 30 (0.00%) 0 |
| Injury, poisoning and procedural complications Arthropod bite subjects affected / exposed occurrences (all) Procedural pain subjects affected / exposed occurrences (all) | 1 / 35 (2.86%) 1 0 / 35 (0.00%) 0 | 0 / 48 (0.00%) 0 0 / 48 (0.00%) 0 | 0 / 30 (0.00%) 0 4 / 30 (13.33%) 4 |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Hypoaesthesia subjects affected / exposed occurrences (all) | 0 / 35 (0.00%) 0 2 / 35 (5.71%) 2 1 / 35 (2.86%) 1 | 2 / 48 (4.17%) 2 5 / 48 (10.42%) 6 0 / 48 (0.00%) 0 | 0 / 30 (0.00%) 0 1 / 30 (3.33%) 1 0 / 30 (0.00%) 0 |
| General disorders and administration site conditions | | | |

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

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

| | | | |
|--|----------------------|----------------------|---------------------|
| Tooth abscess subjects affected / exposed occurrences (all) | 1 / 35 (2.86%) 1 | 0 / 48 (0.00%) 0 | 1 / 30 (3.33%) 1 |
| Sinusitis subjects affected / exposed occurrences (all) | 2 / 35 (5.71%) 3 | 1 / 48 (2.08%) 1 | 0 / 30 (0.00%) 0 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 1 / 35 (2.86%) 1 | 0 / 48 (0.00%) 0 | 2 / 30 (6.67%) 2 |
| Metabolism and nutrition disorders Diabetes mellitus inadequate control subjects affected / exposed occurrences (all) | 6 / 35 (17.14%) 6 | 5 / 48 (10.42%) 5 | 2 / 30 (6.67%) 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 occurrences (all) | 3 / 31 (9.68%) 3 | | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Injury, poisoning and procedural complications Arthropod bite subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Procedural pain subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 2 / 31 (6.45%) 2 | | |
| Headache | | | |

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