



Clinical trial results:

Long Term Safety Study of PRALUENT in Patients with Heterozygous Familial Hypercholesterolemia or with Non-Familial Hypercholesterolemia at High and Very High Cardiovascular Risk and Previously Enrolled in the Neurocognitive Function Trial

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2018-002810-11 |
| Trial protocol | EE BG |
| Global end of trial date | 08 April 2020 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 |
| This version publication date | 23 April 2021 |
| First version publication date | 23 April 2021 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | R727-CL-1609 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03694197 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--------------------------------------------------------------------------------------------------------------|
| Sponsor organisation name | Regeneron Pharmaceuticals, Inc. |
| Sponsor organisation address | 777 Old Saw Mill River Rd., Tarrytown, NY, United States, 10591 |
| Public contact | Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 8447346643, clinicaltrials@regeneron.com |
| Scientific contact | Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 8447346643, clinicaltrials@regeneron.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 | 08 April 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 08 April 2020 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the long term safety of PRALUENT in subjects with heterozygous familial hypercholesterolemia (heFH) or non-familial hypercholesterolemia (FH) subjects at high or very high cardiovascular risk who completed the neurocognitive function study R727-CL-1532 (2016-003189-16).

The secondary objectives of the study were:

- To evaluate the effect of PRALUENT on low-density lipoprotein cholesterol (LDL-C)
- To evaluate the effect of PRALUENT on other lipid parameters
- To evaluate the effect of PRALUENT on gonadal steroid hormones

Protection of trial subjects:

This clinical study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with the International Council for Harmonisation (ICH) guidelines for GCP and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

| | |
|-----------------------------------------------------------|-------------------|
| Actual start date of recruitment | 28 September 2018 |
| 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: 96 |
| Country: Number of subjects enrolled | Estonia: 39 |
| Country: Number of subjects enrolled | Russian Federation: 260 |
| Country: Number of subjects enrolled | South Africa: 304 |
| Country: Number of subjects enrolled | Ukraine: 276 |
| Country: Number of subjects enrolled | United States: 410 |
| Worldwide total number of subjects | 1385 |
| EEA total number of subjects | 135 |

Notes:

Subjects enrolled per age group

| | |
|----------------------------------------|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 | 0 |

| | |
|------------------------------------------|-----|
| wk | |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 680 |
| From 65 to 84 years | 702 |
| 85 years and over | 3 |

Subject disposition

Recruitment

Recruitment details:

The 1389 subjects who completed double-blind treatment and the end-of-study (EOS) visit in R727-CL-1532 (2016-003189-16) signed consent and were screened for this open-label study (EOS visit corresponded to day 1/visit 1 of this study).

Pre-assignment

Screening details:

First subcutaneous (SC) injection was administered in the clinic (day 1/visit 1). Four of the 1389 subjects discontinued on day 1 before treatment: 2 discontinued due to failure to meet inclusion/exclusion criteria, 1 withdrew consent, and 1 discontinued due to adverse event (AE). A total of 1385 subjects received any study drug on day 1.

Period 1

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

Arms

| | |
|-----------|-----------------------------|
| Arm title | Alirocumab 75 Q2W/Up150 Q2W |
|-----------|-----------------------------|

Arm description:

All subjects initiated treatment with PRALUENT (alirocumab) at the starting dose of 75 milligrams (mg) once every 2 weeks (Q2W). After week 8, the dose could be adjusted (up to 150 mg Q2W, maintained or from 150 mg Q2W to 75 mg Q2W) if needed based on low-density lipoprotein cholesterol (LDL-C) levels.

| | |
|----------------------------------------|------------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Alirocumab |
| Investigational medicinal product code | SUB74847 |
| Other name | PRALUENT |
| Pharmaceutical forms | Solution for injection in pre-filled pen |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

75mg

| Number of subjects in period 1 | Alirocumab 75 Q2W/Up150 Q2W |
|---------------------------------------------|-----------------------------|
| Started | 1385 |
| Completed | 0 |
| Not completed | 1385 |
| Physician decision | 4 |
| Subject withdrew consent | 10 |
| Protocol became inconvenient to participate | 1 |
| Related to IMP administration | 1 |
| Adverse event, non-fatal | 9 |
| Study terminated by sponsor | 1350 |
| Subject moved | 5 |

| | |
|---------------|---|
| Not disclosed | 5 |
|---------------|---|

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------------------------|
| Reporting group title | Alirocumab 75 Q2W/Up150 Q2W |
|-----------------------|-----------------------------|

Reporting group description:

All subjects initiated treatment with PRALUENT (alirocumab) at the starting dose of 75 milligrams (mg) once every 2 weeks (Q2W). After week 8, the dose could be adjusted (up to 150 mg Q2W, maintained or from 150 mg Q2W to 75 mg Q2W) if needed based on low-density lipoprotein cholesterol (LDL-C) levels.

| Reporting group values | Alirocumab 75 Q2W/Up150 Q2W | Total | |
|-------------------------------------------|-----------------------------|-------|--|
| Number of subjects | 1385 | 1385 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 680 | 680 | |
| From 65-84 years | 702 | 702 | |
| 85 years and over | 3 | 3 | |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 64.6 | | |
| standard deviation | ± 8.63 | - | |
| Sex: Female, Male | | | |
| Units: Subjects | | | |
| Female | 527 | 527 | |
| Male | 858 | 858 | |
| Race/Ethnicity, Customized | | | |
| Race | | | |
| Units: Subjects | | | |
| White | 1178 | 1178 | |
| Black or African American | 81 | 81 | |
| Asian | 7 | 7 | |
| American Indian or Alaska Native | 1 | 1 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Other | 118 | 118 | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 10 | 10 | |
| Not Hispanic or Latino | 1372 | 1372 | |
| Unknown or Not Reported | 3 | 3 | |

End points

End points reporting groups

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|
| Reporting group title | Alirocumab 75 Q2W/Up150 Q2W |
| Reporting group description: | |
| All subjects initiated treatment with PRALUENT (alirocumab) at the starting dose of 75 milligrams (mg) once every 2 weeks (Q2W). After week 8, the dose could be adjusted (up to 150 mg Q2W, maintained or from 150 mg Q2W to 75 mg Q2W) if needed based on low-density lipoprotein cholesterol (LDL-C) levels. | |

Primary: Number of subjects with adverse events (AE) after first administration of study drug through the last dose of study drug plus 2 weeks

| | |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of subjects with adverse events (AE) after first administration of study drug through the last dose of study drug plus 2 weeks ^[1] |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

An AE is any untoward medical occurrence in a participant administered a study drug which may or may not have a causal relationship with the study drug. AEs include serious adverse events (SAEs), AEs leading to treatment discontinuation, and adverse events of special interest (AESI). AESI include local injection site reactions, general allergic events, elevated alanine aminotransferase (ALT) levels greater than or equal to (\geq) 3 upper limit normal (ULN) (if baseline is less than ($<$) ULN)/ALT $\geq 2 \times$ ULN (if baseline \geq ULN), neurologic events, neurocognitive events (according to Customized Medical Dictionary for Regulatory Activities [MedDRA] Query [CMQ] by Sponsor grouping and CMQ by FDA grouping), cataract, new onset diabetes (NOD), hepatic disorders, and diabetes mellitus (DM)/diabetic complications.

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

End point timeframe:

After first administration of study drug through the last dose of study drug plus 2 weeks; Safety analysis set (SAF): All subjects who received any study drug

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal inferential testing was performed

| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
|----------------------------------------------------|-----------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: Subjects | | | | |
| Any treatment emergent AE (TEAE) | 568 | | | |
| Any treatment emergent serious AE (SAE) | 89 | | | |
| Any TEAE leading to death | 5 | | | |
| Any TEAE leading to perm. treatment discount. | 9 | | | |
| Any neurocognitive disorders TEAE (by Sponsor CMQ) | 4 | | | |
| Any neurocognitive disorders TEAE (by FDA CMQ) | 0 | | | |
| Any NOD; n=687 (w/out diabetes at baseline) | 15 | | | |
| Any hepatic disorders TEAE | 14 | | | |
| Any neurological TEAE | 15 | | | |
| Any general allergic TEAE | 25 | | | |

| | | | | |
|----------------------------------------------------|----|--|--|--|
| At least one TE injection site reaction | 22 | | | |
| Any cataract TEAE | 5 | | | |
| Any elevated ALT ≥ 3 ULN | 1 | | | |
| Any DM/DC TEAE; n=698 (with diabetes at baseline) | 41 | | | |
| Any DM/DC TEAE; n=687 (w/out diabetes at baseline) | 3 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Calculated low-density lipoprotein cholesterol (LDL-C) values from baseline over time

| | |
|-----------------|---------------------------------------------------------------------------------------|
| End point title | Calculated low-density lipoprotein cholesterol (LDL-C) values from baseline over time |
|-----------------|---------------------------------------------------------------------------------------|

End point description:

The baseline value was defined as the last available value before the first dose of double-blind study treatment in study R727-CL-1532 (2016-003189-16); Safety analysis set (SAF): All subjects who received any study drug; Here, "n" = number of subjects evaluable at that timepoint

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

End point timeframe:

Up to week 72

| | | | | |
|-----------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: Milligrams per decilitre (mg/dL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 1367) | 117.8 (\pm 40.67) | | | |
| Week 8 (n = 1345) | 58.9 (\pm 37.31) | | | |
| Week 12 (n = 356) | 63.6 (\pm 40.79) | | | |
| Week 24 (n = 769) | 56.2 (\pm 36.59) | | | |
| Week 48 (n = 311) | 56.8 (\pm 36.13) | | | |
| Week 72 (n = 54) | 52.2 (\pm 38.80) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in LDL-C from baseline over time

| | |
|-----------------|-------------------------------------------------|
| End point title | Percent change in LDL-C from baseline over time |
|-----------------|-------------------------------------------------|

End point description:

SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint

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

End point timeframe:

Up to week 72

| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
|--------------------------------------|-----------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: Percent Change | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8 (n = 1328) | -48.74 (± 31.121) | | | |
| Week 12 (n = 353) | -44.64 (± 35.338) | | | |
| Week 24 (n = 754) | -50.75 (± 30.249) | | | |
| Week 48 (n = 301) | -52.35 (± 27.929) | | | |
| Week 72 (n = 54) | -51.21 (± 32.742) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Total cholesterol (Total-C) values from baseline over time

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|-----------------|------------------------------------------------------------|
| End point title | Total cholesterol (Total-C) values from baseline over time |
|-----------------|------------------------------------------------------------|

End point description:

The baseline value was defined as the last available value before the first dose of double-blind study treatment in study R727-CL-1532 (2016-003189-16); SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint

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

End point timeframe:

Up to week 72

| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
|--------------------------------------|-----------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |

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|---------------------|-----------------|--|--|--|
| Baseline (n = 1385) | 199.5 (± 48.88) | | | |
| Week 8 (n = 1346) | 139.5 (± 44.76) | | | |
| Week 12 (n = 356) | 145.0 (± 48.68) | | | |
| Week 24 (n = 769) | 137.3 (± 44.18) | | | |
| Week 48 (n = 311) | 139.5 (± 44.53) | | | |
| Week 72 (n = 54) | 131.7 (± 43.25) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline in Total-C over time

| | |
|--------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| End point title | Percent change from baseline in Total-C over time |
| End point description: SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint | |
| End point type | Secondary |
| End point timeframe: Up to week 72 | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: Percent Change | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8 (n = 1346) | -28.68 (± 20.158) | | | |
| Week 12 (n = 356) | -25.99 (± 23.058) | | | |
| Week 24 (n = 769) | -29.98 (± 20.930) | | | |
| Week 48 (n = 311) | -30.89 (± 21.004) | | | |
| Week 72 (n = 54) | -31.55 (± 22.238) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Lipoprotein-a (Lp(a)) values from baseline over time

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|-----------------|------------------------------------------------------|
| End point title | Lipoprotein-a (Lp(a)) values from baseline over time |
|-----------------|------------------------------------------------------|

End point description:

The baseline value was defined as the last available value before the first dose of double-blind study treatment in study R727-CL-1532 (2016-003189-16); SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint

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

End point timeframe:

Up to week 72

| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
|--------------------------------------|-----------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 1385) | 39.7 (± 47.86) | | | |
| Week 8 (n = 190) | 35.0 (± 41.99) | | | |
| Week 12 (n = 353) | 32.7 (± 39.42) | | | |
| Week 24 (n = 419) | 33.9 (± 42.54) | | | |
| Week 48 (n = 311) | 38.6 (± 50.66) | | | |
| Week 72 (n = 54) | 40.4 (± 56.47) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline in Lp(a) over time

| | |
|-----------------|-------------------------------------------------|
| End point title | Percent change from baseline in Lp(a) over time |
|-----------------|-------------------------------------------------|

End point description:

SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint

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

End point timeframe:

Up to week 72

| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
|--------------------------------------|-----------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: Percent Change | | | | |
| arithmetic mean (standard deviation) | | | | |

| | | | | |
|-------------------|-------------------|--|--|--|
| Week 8 (n = 190) | -12.69 (± 35.452) | | | |
| Week 12 (n = 353) | 10.63 (± 228.659) | | | |
| Week 24 (n = 419) | -6.80 (± 110.827) | | | |
| Week 48 (n = 311) | -7.89 (± 116.831) | | | |
| Week 72 (n = 54) | -22.23 (± 28.233) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Non-high-density lipoprotein cholesterol (non-HDL-C) values from baseline over time

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|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| End point title | Non-high-density lipoprotein cholesterol (non-HDL-C) values from baseline over time |
| End point description: The baseline value was defined as the last available value before the first dose of double-blind study treatment in study R727-CL-1532 (2016-003189-16); SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint | |
| End point type | Secondary |
| End point timeframe: Up to week 72 | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 1385) | 152.4 (± 48.81) | | | |
| Week 8 (n = 1346) | 88.5 (± 43.54) | | | |
| Week 12 (n = 356) | 94.3 (± 48.77) | | | |
| Week 24 (n = 769) | 87.3 (± 43.56) | | | |
| Week 48 (n = 311) | 88.9 (± 44.25) | | | |
| Week 72 (n = 54) | 80.9 (± 42.67) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline in non-HDL-C over time

| | |
|--------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|
| End point title | Percent change from baseline in non-HDL-C over time |
| End point description: SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint | |
| End point type | Secondary |
| End point timeframe: Up to week 72 | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: Percent Change | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8 (n = 1346) | -40.35 (± 27.470) | | | |
| Week 12 (n = 356) | -36.89 (± 29.567) | | | |
| Week 24 (n = 769) | -41.47 (± 26.763) | | | |
| Week 48 (n = 311) | -42.33 (± 28.728) | | | |
| Week 72 (n = 54) | -43.28 (± 29.534) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: High-density lipoprotein cholesterol (HDL-C) values from baseline over time

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|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| End point title | High-density lipoprotein cholesterol (HDL-C) values from baseline over time |
| End point description: The baseline value was defined as the last available value before the first dose of double-blind study treatment in study R727-CL-1532 (2016-003189-16); SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint | |
| End point type | Secondary |
| End point timeframe: Up to week 72 | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 1385) | 47.1 (± 13.92) | | | |
| Week 8 (n = 1346) | 51.0 (± 14.82) | | | |
| Week 12 (n = 356) | 50.6 (± 13.95) | | | |
| Week 24 (n = 769) | 49.9 (± 14.80) | | | |
| Week 48 (n = 311) | 50.5 (± 14.66) | | | |
| Week 72 (n = 54) | 50.8 (± 14.61) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline in HDL-C over time

| | |
|--------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|
| End point title | Percent change from baseline in HDL-C over time |
| End point description: SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint | |
| End point type | Secondary |
| End point timeframe: Up to week 72 | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: Percent Change | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8 (n = 1346) | 10.54 (± 22.735) | | | |
| Week 12 (n = 356) | 10.33 (± 21.933) | | | |
| Week 24 (n = 769) | 8.53 (± 21.824) | | | |
| Week 48 (n = 311) | 9.81 (± 23.690) | | | |
| Week 72 (n = 54) | 9.24 (± 21.505) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Fasting triglycerides (TGs) values from baseline over time

| | |
|-----------------|------------------------------------------------------------|
| End point title | Fasting triglycerides (TGs) values from baseline over time |
|-----------------|------------------------------------------------------------|

End point description:

The baseline value was defined as the last available value before the first dose of double-blind study treatment in study R727-CL-1532 (2016-003189-16); SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint

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

End point timeframe:

Up to week 72

| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
|--------------------------------------|-----------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 1385) | 179.2 (± 146.51) | | | |
| Week 8 (n = 1346) | 154.8 (± 113.05) | | | |
| Week 12 (n = 356) | 162.2 (± 182.00) | | | |
| Week 24 (n = 769) | 169.3 (± 161.45) | | | |
| Week 48 (n = 311) | 171.1 (± 131.35) | | | |
| Week 72 (n = 54) | 156.9 (± 65.21) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline in fasting TGs over time

| | |
|-----------------|-------------------------------------------------------|
| End point title | Percent change from baseline in fasting TGs over time |
|-----------------|-------------------------------------------------------|

End point description:

SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint

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

End point timeframe:

Up to week 72

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: Percent Change | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8 (n = 1346) | -4.68 (± 49.230) | | | |
| Week 12 (n = 356) | -4.29 (± 40.748) | | | |
| Week 24 (n = 769) | 0.42 (± 54.118) | | | |
| Week 48 (n = 311) | 1.54 (± 69.156) | | | |
| Week 72 (n = 54) | -5.97 (± 41.440) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Apolipoprotein B (Apo B) values from baseline over time

| | |
|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Apolipoprotein B (Apo B) values from baseline over time |
| End point description: | The baseline value was defined as the last available value before the first dose of double-blind study treatment in study R727-CL-1532 (2016-003189-16). SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint |
| End point type | Secondary |
| End point timeframe: | Up to week 72 |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 1385) | 103.8 (± 27.25) | | | |
| Week 8 (n = 190) | 62.5 (± 27.63) | | | |
| Week 12 (n = 353) | 68.0 (± 31.32) | | | |
| Week 24 (n = 420) | 61.5 (± 26.20) | | | |
| Week 48 (n = 311) | 63.7 (± 26.40) | | | |
| Week 72 (n = 54) | 58.5 (± 25.82) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline in Apo B over time

| | |
|--------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|
| End point title | Percent change from baseline in Apo B over time |
| End point description: SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint | |
| End point type | Secondary |
| End point timeframe: Up to week 72 | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: Percent Change | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8 (n = 190) | -36.51 (± 34.460) | | | |
| Week 12 (n = 353) | -34.48 (± 27.905) | | | |
| Week 24 (n = 420) | -38.16 (± 24.867) | | | |
| Week 48 (n = 311) | -37.93 (± 23.767) | | | |
| Week 72 (n = 54) | -39.04 (± 26.383) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Apolipoprotein-A1 (Apo A1) values from baseline over time

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| End point title | Apolipoprotein-A1 (Apo A1) values from baseline over time |
| End point description: The baseline value was defined as the last available value before the first dose of double-blind study treatment in study R727-CL-1532 (2016-003189-16). SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint | |
| End point type | Secondary |
| End point timeframe: Up to week 72 | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 1385) | 145.3 (± 24.95) | | | |
| Week 8 (n = 190) | 148.5 (± 24.73) | | | |
| Week 12 (n = 353) | 149.4 (± 25.38) | | | |
| Week 24 (n = 420) | 150.7 (± 26.36) | | | |
| Week 48 (n = 311) | 152.6 (± 25.96) | | | |
| Week 72 (n = 54) | 151.4 (± 26.03) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline in Apo A1 over time

| | |
|------------------------------------------------------------------------------------------------------------|--------------------------------------------------|
| End point title | Percent change from baseline in Apo A1 over time |
| End point description: | |
| SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint | |
| End point type | Secondary |
| End point timeframe: | |
| Up to week 72 | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: Percent Change | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8 (n = 190) | 5.07 (± 13.385) | | | |
| Week 12 (n = 353) | 2.99 (± 13.638) | | | |
| Week 24 (n = 420) | 5.35 (± 14.108) | | | |
| Week 48 (n = 311) | 4.77 (± 13.836) | | | |
| Week 72 (n = 54) | 1.21 (± 13.170) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Gonadal hormone (follicle stimulating hormone [FSH] and luteinizing hormone [LH]) values for female subjects from baseline over time

| | |
|------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Gonadal hormone (follicle stimulating hormone [FSH] and luteinizing hormone [LH]) values for female subjects from baseline over time |
| End point description: | The baseline value was defined as the last available value before the first dose of double-blind study treatment in study R727-CL-1532 (2016-003189-16); SAF (Female subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint |
| End point type | Secondary |
| End point timeframe: | Up to week 72 |

| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
|---------------------------------------------|-----------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 527 | | | |
| Units: International units per litre (IU/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| FSH Baseline (n = 527) | 57.948 (± 26.7383) | | | |
| FSH Week 8 (n = 84) | 59.264 (± 24.7912) | | | |
| FSH Week 12 (n = 135) | 54.279 (± 23.9923) | | | |
| FSH Week 24 (n = 280) | 57.664 (± 25.9830) | | | |
| FSH Week 48 (n = 106) | 56.529 (± 25.1408) | | | |
| FSH Week 72 (n = 23) | 58.600 (± 24.5205) | | | |
| LH Baseline (n = 527) | 30.155 (± 13.1090) | | | |
| LH Week 8 (n = 84) | 33.794 (± 14.4459) | | | |
| LH Week 12 (n = 135) | 30.779 (± 13.0946) | | | |
| LH Week 24 (n = 280) | 31.260 (± 13.7344) | | | |
| LH Week 48 (n = 106) | 29.585 (± 13.9792) | | | |
| LH Week 72 (n = 23) | 29.248 (± 11.0829) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in gonadal hormones (FSH and LH) for female subjects over time

| | |
|-----------------|-------------------------------------------------------------------------------------|
| End point title | Change from baseline in gonadal hormones (FSH and LH) for female subjects over time |
|-----------------|-------------------------------------------------------------------------------------|

End point description:

SAF (Female subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint

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

End point timeframe:

Up to week 72

| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
|--------------------------------------|-----------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 527 | | | |
| Units: IU/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| FSH Week 8 (n = 84) | -0.765 (± 12.0083) | | | |
| FSH Week 12 (n = 135) | -0.984 (± 12.1584) | | | |
| FSH Week 24 (n = 280) | -0.575 (± 8.7780) | | | |
| FSH Week 48 (n = 106) | -0.877 (± 15.9972) | | | |
| FSH Week 72 (n = 23) | -1.861 (± 8.6119) | | | |
| LH Week 8 (n = 84) | 2.730 (± 8.2258) | | | |
| LH Week 12 (n = 135) | 1.882 (± 8.2884) | | | |
| LH Week 24 (n = 280) | 0.939 (± 6.3694) | | | |
| LH Week 48 (n = 106) | 0.367 (± 8.5631) | | | |
| LH Week 72 (n = 23) | 0.222 (± 6.8910) | | | |

Statistical analyses

Secondary: Gonadal (FSH and LH) hormone values for male subjects from baseline over time

| | |
|-----------------|-------------------------------------------------------------------------------|
| End point title | Gonadal (FSH and LH) hormone values for male subjects from baseline over time |
|-----------------|-------------------------------------------------------------------------------|

End point description:

The baseline value was defined as the last available value before the first dose of double-blind study treatment in study R727-CL-1532 (2016-003189-16); SAF (Male subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint

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

End point timeframe:

Up to week 72

| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
|---------------------------------------------|-----------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 858 | | | |
| Units: International units per litre (IU/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| FSH Baseline (n = 858) | 8.006 (± 7.4451) | | | |
| FSH Week 8 (n = 117) | 7.959 (± 7.5500) | | | |
| FSH Week 12 (n = 215) | 7.766 (± 6.8204) | | | |
| FSH Week 24 (n = 489) | 8.268 (± 8.1355) | | | |
| FSH Week 48 (n = 203) | 9.597 (± 11.2138) | | | |
| FSH Week 72 (n = 32) | 10.005 (± 13.2973) | | | |
| LH Baseline (n = 858) | 6.500 (± 4.2832) | | | |
| LH Week 8 (n = 117) | 7.094 (± 4.7226) | | | |
| LH Week 12 (n = 215) | 6.688 (± 4.4079) | | | |
| LH Week 24 (n = 489) | 6.931 (± 4.8597) | | | |
| LH Week 48 (n = 203) | 7.677 (± 6.5478) | | | |
| LH Week 72 (n = 32) | 8.173 (± 8.9083) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in gonadal hormones (FSH and LH) for male subjects over time

| | |
|---------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|
| End point title | Change from baseline in gonadal hormones (FSH and LH) for male subjects over time |
| End point description: SAF (Male subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint | |
| End point type | Secondary |
| End point timeframe: Up to week 72 | |

| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
|--------------------------------------|-----------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 858 | | | |
| Units: IU/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| FSH Week 8 (n = 117) | 0.285 (± 3.7264) | | | |
| FSH Week 12 (n = 215) | -0.598 (± 4.1076) | | | |
| FSH Week 24 (n = 489) | 0.331 (± 6.0522) | | | |
| FSH Week 48 (n = 203) | 0.960 (± 10.3803) | | | |
| FSH Week 72 (n = 32) | 2.458 (± 13.4730) | | | |
| LH Week 8 (n = 117) | 0.535 (± 2.4847) | | | |
| LH Week 12 (n = 215) | -0.136 (± 3.2638) | | | |
| LH Week 24 (n = 489) | 0.582 (± 4.4964) | | | |
| LH Week 48 (n = 203) | 1.015 (± 6.6344) | | | |
| LH Week 72 (n = 32) | 1.964 (± 9.3028) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Gonadotropin (estradiol) values for female subjects from baseline over time

| | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| End point title | Gonadotropin (estradiol) values for female subjects from baseline over time |
| End point description: The baseline value was defined as the last available value before the first dose of double-blind study treatment in study R727-CL-1532 (2016-003189-16); SAF (Female subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint | |
| End point type | Secondary |
| End point timeframe: Up to week 72 | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 527 | | | |
| Units: picomoles per litre (pmol/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 527) | 55.589 (\pm 80.8238) | | | |
| Week 8 (n = 84) | 58.676 (\pm 69.0119) | | | |
| Week 12 (n = 135) | 59.673 (\pm 74.7587) | | | |
| Week 24 (n = 280) | 64.304 (\pm 103.8955) | | | |
| Week 48 (n = 106) | 64.503 (\pm 102.1595) | | | |
| Week 72 (n = 23) | 57.926 (\pm 67.1795) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in gonadotropins (estradiol) for female subjects over time

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------|
| End point title | Change from baseline in gonadotropins (estradiol) for female subjects over time |
| End point description: SAF (Female subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint | |
| End point type | Secondary |
| End point timeframe: Up to week 72 | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 527 | | | |
| Units: pmol/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8 (n = 84) | 4.272 (\pm 77.1561) | | | |
| Week 12 (n = 135) | 9.262 (\pm 73.1050) | | | |

| | | | | |
|-------------------|-------------------------|--|--|--|
| Week 24 (n = 280) | 7.869 (\pm 78.4151) | | | |
| Week 48 (n = 106) | 11.763 (\pm 97.5350) | | | |
| Week 72 (n = 23) | 9.569 (\pm 38.0952) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Gonadotropin (testosterone) values for male subjects from baseline over time

| | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| End point title | Gonadotropin (testosterone) values for male subjects from baseline over time |
| End point description: The baseline value was defined as the last available value before the first dose of double-blind study treatment in study R727-CL-1532 (2016-003189-16); SAF (Male subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint | |
| End point type | Secondary |
| End point timeframe: Up to week 72 | |

| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
|--------------------------------------|-----------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 858 | | | |
| Units: nanomoles per litre (nmol/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 858) | 13.4370 (\pm 6.36321) | | | |
| Week 8 (n = 117) | 14.5802 (\pm 5.99821) | | | |
| Week 12 (n = 215) | 14.2443 (\pm 6.77070) | | | |
| Week 24 (n = 489) | 13.5818 (\pm 6.11269) | | | |
| Week 48 (n = 203) | 13.4798 (\pm 7.04977) | | | |
| Week 72 (n = 32) | 12.7538 (\pm 6.37408) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in gonadotropins (testosterone) for male subjects over time

| | |
|---------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| End point title | Change from baseline in gonadotropins (testosterone) for male subjects over time |
| End point description: SAF (Male subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint | |
| End point type | Secondary |
| End point timeframe: Up to week 72 | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 858 | | | |
| Units: nmol/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8 (n = 117) | 0.6030 (± 4.46401) | | | |
| Week 12 (n = 215) | 0.7965 (± 4.74765) | | | |
| Week 24 (n = 489) | 0.1946 (± 5.89220) | | | |
| Week 48 (n = 203) | 0.0498 (± 6.34201) | | | |
| Week 72 (n = 32) | 1.2569 (± 5.29335) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Alanine aminotransferase values from baseline over time

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------|
| End point title | Alanine aminotransferase values from baseline over time |
| End point description: The baseline value was defined as the last available value before the first dose of double-blind study treatment in study R727-CL-1532 (2016-003189-16); SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint | |
| End point type | Secondary |
| End point timeframe: Up to week 72 | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: Upper limit of normal (ULN) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 1385) | 0.516 (± 0.3218) | | | |
| Week 8 (n = 201) | 0.468 (± 0.2745) | | | |
| Week 12 (n = 350) | 0.505 (± 0.4940) | | | |
| Week 24 (n = 769) | 0.493 (± 0.2851) | | | |
| Week 48 (n = 310) | 0.533 (± 0.3267) | | | |
| Week 72 (n = 54) | 0.468 (± 0.2340) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in alanine aminotransferase over time

| | |
|------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|
| End point title | Change from baseline in alanine aminotransferase over time |
| End point description: | |
| SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint | |
| End point type | Secondary |
| End point timeframe: | |
| Up to week 72 | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: ULN | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8 (n = 201) | -0.025 (± 0.3006) | | | |
| Week 12 (n = 350) | 0.009 (± 0.5189) | | | |
| Week 24 (n = 769) | -0.036 (± 0.3294) | | | |
| Week 48 (n = 310) | -0.027 (± 0.3052) | | | |
| Week 72 (n = 54) | -0.062 (± 0.1872) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Aspartate aminotransferase values from baseline over time

| | |
|-----------------|-----------------------------------------------------------|
| End point title | Aspartate aminotransferase values from baseline over time |
|-----------------|-----------------------------------------------------------|

End point description:

The baseline value was defined as the last available value before the first dose of double-blind study treatment in study R727-CL-1532 (2016-003189-16); SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint

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

End point timeframe:

Up to week 72

| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
|--------------------------------------|-----------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: ULN | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 1385) | 0.553 (± 0.2516) | | | |
| Week 8 (n = 201) | 0.520 (± 0.2536) | | | |
| Week 12 (n = 350) | 0.527 (± 0.2698) | | | |
| Week 24 (n = 769) | 0.544 (± 0.3071) | | | |
| Week 48 (n = 310) | 0.565 (± 0.2773) | | | |
| Week 72 (n = 54) | 0.556 (± 0.2256) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in aspartate aminotransferase over time

| | |
|-----------------|--------------------------------------------------------------|
| End point title | Change from baseline in aspartate aminotransferase over time |
|-----------------|--------------------------------------------------------------|

End point description:

SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to week 72 | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: ULN | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8 (n = 201) | -0.022 (± 0.2856) | | | |
| Week 12 (n = 350) | -0.017 (± 0.3004) | | | |
| Week 24 (n = 769) | -0.013 (± 0.2901) | | | |
| Week 48 (n = 310) | -0.019 (± 0.2390) | | | |
| Week 72 (n = 54) | -0.037 (± 0.1730) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Alkaline phosphatase values from baseline over time

| | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|
| End point title | Alkaline phosphatase values from baseline over time |
| End point description: | |
| The baseline value was defined as the last available value before the first dose of double-blind study treatment in study R727-CL-1532 (2016-003189-16); SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint | |
| End point type | Secondary |
| End point timeframe: | |
| Up to week 72 | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: ULN | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 1385) | 0.601 (± 0.1865) | | | |
| Week 8 (n = 201) | 0.635 (± 0.2151) | | | |

| | | | | |
|-------------------|------------------|--|--|--|
| Week 12 (n = 350) | 0.605 (± 0.1865) | | | |
| Week 24 (n = 769) | 0.602 (± 0.2012) | | | |
| Week 48 (n = 310) | 0.602 (± 0.2657) | | | |
| Week 72 (n = 54) | 0.553 (± 0.1678) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in alkaline phosphatase over time

| | |
|--------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------|
| End point title | Change from baseline in alkaline phosphatase over time |
| End point description: SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint | |
| End point type | Secondary |
| End point timeframe: Up to week 72 | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: ULN | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8 (n = 201) | 0.009 (± 0.1371) | | | |
| Week 12 (n = 350) | 0.013 (± 0.1203) | | | |
| Week 24 (n = 769) | 0.006 (± 0.1152) | | | |
| Week 48 (n = 310) | 0.024 (± 0.2333) | | | |
| Week 72 (n = 54) | -0.011 (± 0.1029) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Total bilirubin values from baseline over time

| | |
|----------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------|
| End point title | Total bilirubin values from baseline over time |
| End point description: The baseline value was defined as the last available value before the first dose of double-blind study | |

treatment in study R727-CL-1532 (2016-003189-16); SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to week 72 | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: micromoles per litre (umol/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 1385) | 10.76 (± 4.736) | | | |
| Week 8 (n = 201) | 10.01 (± 4.123) | | | |
| Week 12 (n = 350) | 10.26 (± 4.758) | | | |
| Week 24 (n = 769) | 10.41 (± 4.922) | | | |
| Week 48 (n = 310) | 10.06 (± 4.503) | | | |
| Week 72 (n = 54) | 8.82 (± 3.770) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in total bilirubin over time

| | |
|------------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| End point title | Change from baseline in total bilirubin over time |
| End point description: | |
| SAF (All subjects who received any study drug); Here, "n" = number of subjects evaluable at that timepoint | |
| End point type | Secondary |
| End point timeframe: | |
| Up to week 72 | |

| | | | | |
|--------------------------------------|-----------------------------|--|--|--|
| End point values | Alirocumab 75 Q2W/Up150 Q2W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1385 | | | |
| Units: umol/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8 (n = 201) | -0.37 (± 3.120) | | | |

| | | | | |
|-------------------|-----------------|--|--|--|
| Week 12 (n = 350) | -0.44 (± 3.854) | | | |
| Week 24 (n = 769) | -0.48 (± 3.962) | | | |
| Week 48 (n = 310) | -0.05 (± 3.991) | | | |
| Week 72 (n = 54) | 0.71 (± 2.152) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Adverse events (AEs) were recorded from the time of signed informed consent until the end of study.

Adverse event reporting additional description:

Treatment-emergent adverse events (TEAEs) are reported. TEAEs are AEs that developed or worsened or became serious during the TEAE period (time from first dose of study drug to the last study visit).

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
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| | |
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| Dictionary version | 23.0 |
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Reporting groups

| | |
|-----------------------|-----------------------------|
| Reporting group title | Alirocumab 75 Q2W/Up150 Q2W |
|-----------------------|-----------------------------|

Reporting group description:

All subjects initiated treatment with PRALUENT (alirocumab) at the starting dose of 75 milligrams (mg) once every 2 weeks (Q2W). After week 8, the dose could be adjusted (up to 150 mg Q2W, maintained or from 150 mg Q2W to 75 mg Q2W) if needed based on low-density lipoprotein cholesterol (LDL-C) levels.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No occurrence of non-serious adverse events met the 5% threshold for reporting

| Serious adverse events | Alirocumab 75 Q2W/Up150 Q2W | | |
|---------------------------------------------------------------------|-----------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 89 / 1385 (6.43%) | | |
| number of deaths (all causes) | 5 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Prostate cancer | | | |
| subjects affected / exposed | 2 / 1385 (0.14%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Synovial sarcoma | | | |

| | | | |
|------------------------------------------------------|------------------|--|--|
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypertensive urgency | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peripheral artery occlusion | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 3 / 1385 (0.22%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Death | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |

| | | | |
|-------------------------------------------------|------------------|--|--|
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Uterine polyp | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchitis chronic | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Paranasal cyst | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Bipolar disorder | | | |

| | | | |
|-------------------------------------------------|------------------|--|--|
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Arterial injury | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cartilage injury | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Concussion | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Electric shock | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fall | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lower limb fracture | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Traumatic haemorrhage | | | |

| | | | |
|-------------------------------------------------|-------------------|--|--|
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Cardiac disorders | | | |
| Angina unstable | | | |
| subjects affected / exposed | 10 / 1385 (0.72%) | | |
| occurrences causally related to treatment / all | 0 / 10 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Angina pectoris | | | |
| subjects affected / exposed | 8 / 1385 (0.58%) | | |
| occurrences causally related to treatment / all | 0 / 8 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 6 / 1385 (0.43%) | | |
| occurrences causally related to treatment / all | 0 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 5 / 1385 (0.36%) | | |
| occurrences causally related to treatment / all | 0 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute left ventricular failure | | | |
| subjects affected / exposed | 2 / 1385 (0.14%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 2 / 1385 (0.14%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Coronary artery disease | | | |
| subjects affected / exposed | 2 / 1385 (0.14%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Arrhythmia | | | |

| | | | |
|-------------------------------------------------|------------------|--|--|
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac failure acute | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac failure chronic | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Cardiovascular insufficiency | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |

| | | | |
|-------------------------------------------------|------------------|--|--|
| subjects affected / exposed | 2 / 1385 (0.14%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 2 / 1385 (0.14%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Carotid artery disease | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Carotid artery occlusion | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Encephalopathy | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemorrhagic transformation stroke | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Intestinal ischaemia | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatitis | | | |

| | | | |
|-------------------------------------------------|------------------|--|--|
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatitis chronic | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Umbilical hernia | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Diabetic foot | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urticaria | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 2 / 1385 (0.14%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ureterolithiasis | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|-------------------------------------------------|------------------|--|--|
| Musculoskeletal and connective tissue disorders | | | |
| Osteoarthritis | | | |
| subjects affected / exposed | 2 / 1385 (0.14%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 4 / 1385 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abscess limb | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Appendiceal abscess | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Appendicitis perforated | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|-------------------------------------------------|------------------|--|--|
| Cholecystitis infective | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cystitis | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia staphylococcal | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Diabetic metabolic decompensation | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 1385 (0.07%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| | | | |
|----------------------------------------------------------|--------------------------------|--|--|
| Non-serious adverse events | Alirocumab 75 Q2W/Up150 Q2W | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 1385 (0.00%) | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 23 July 2018 | The protocol was amended to align with feedback received from the European Medicines Agency (EMA), and updated for clarity and consistency with R727-CL-1532 (2016-003189-16) neurocognitive function protocol Amendment 5. |
| 17 September 2018 | The protocol was amended to add back text that was inadvertently removed in protocol amendment 1, and to clarify language for blinding, study discontinuation, treatment compliance, adverse event (AE) reporting period, and procedures for reporting serious adverse events (SAEs). |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported