



Clinical trial results:

Efficacy and Safety of Evinacumab in Adult Patients with Severe Hypertriglyceridemia for the Prevention of Recurrent Acute Pancreatitis Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2021-000437-13 |
| Trial protocol | AT NL DE |
| Global end of trial date | 15 February 2023 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 06 March 2024 |
| First version publication date | 06 March 2024 |

Trial information

Trial identification

| | |
|-----------------------|-----------------|
| Sponsor protocol code | R1500-HTG-20118 |
|-----------------------|-----------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Regeneron |
| Sponsor organisation address | 777 Old Saw Mill River Road, Tarrytown, United States, 10591 |
| Public contact | Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 8447346643, clinicaltrials@regeneron.com |
| Scientific contact | Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc, 9144093597 8447346643, donell.carey@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 | 15 February 2023 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|------------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 15 February 2023 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to determine the proportion of patients with elevated TGs, without FCS due to LoF mutations in LPL, and a history of HTG-associated AP* who experience a recurrent episode of AP after treatment with evinacumab versus placebo.

Protection of trial subjects:

This 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 Good Clinical Practice (GCP) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 12 July 2021 |
| 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 | Canada: 2 |
| Country: Number of subjects enrolled | Netherlands: 1 |
| Country: Number of subjects enrolled | United States: 18 |
| Worldwide total number of subjects | 21 |
| EEA total number of subjects | 1 |

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) | 21 |
| From 65 to 84 years | 0 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 40 participants were screened, of which 21 participants met the eligibility criteria and were randomized in 1:1 to receive either evinacumab or matched placebo. The sponsor terminated the study early due to enrollment issues.

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, Monitor, Carer, Data analyst, Assessor |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

Randomized 1:1

| | |
|--|------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Matching placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

First dose on day 1, with subsequent doses administered approximately every 4 weeks (Q4W)

| | |
|------------------|------------|
| Arm title | Evinacumab |
|------------------|------------|

Arm description:

Participants received evinacumab 20 milligrams per kilogram (mg/kg) IV infusion Q4W starting from Day 1 up to 52 weeks.

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

Dosage and administration details:

First dose on day 1, with subsequent doses administered approximately every 4 weeks (Q4W)

| Number of subjects in period 1 | Placebo | Evinacumab |
|---------------------------------------|---------|------------|
| Started | 10 | 11 |
| Completed | 7 | 5 |
| Not completed | 3 | 6 |
| Subject Decision | - | 4 |
| Lost to follow-up | 3 | 2 |

Baseline characteristics

Reporting groups

| | |
|---|------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Randomized 1:1 | |
| Reporting group title | Evinacumab |
| Reporting group description: | |
| Participants received evinacumab 20 milligrams per kilogram (mg/kg) IV infusion Q4W starting from Day 1 up to 52 weeks. | |

| Reporting group values | Placebo | Evinacumab | Total |
|--|---------|------------|-------|
| Number of subjects | 10 | 11 | 21 |
| 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 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 10 | 11 | 21 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 46.0 | 45.3 | - |
| standard deviation | ± 15.22 | ± 9.46 | - |
| Sex: Female, Male | | | |
| Units: participants | | | |
| Female | 3 | 2 | 5 |
| Male | 7 | 9 | 16 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 2 | 3 | 5 |
| Not Hispanic or Latino | 8 | 8 | 16 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 1 | 1 | 2 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 1 | 1 |
| White | 9 | 9 | 18 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 0 |

End points

End points reporting groups

| | |
|---|------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Randomized 1:1 | |
| Reporting group title | Evinacumab |
| Reporting group description: | |
| Participants received evinacumab 20 milligrams per kilogram (mg/kg) IV infusion Q4W starting from Day 1 up to 52 weeks. | |

Primary: Percentage of Participants with at least One Positively Adjudicated Acute Pancreatitis (AP) Episode

| | |
|--|--|
| End point title | Percentage of Participants with at least One Positively Adjudicated Acute Pancreatitis (AP) Episode ^[1] |
| End point description: | |
| Adjudicated AP episode was determined by an independent acute pancreatitis adjudication committee (APAC). Suspected AP episodes was reviewed by 2 independent physicians. Percentage of participants with at least 1 positively adjudicated AP episode during the 52 weeks was reported. | |
| End point type | Primary |
| End point timeframe: | |
| Baseline to 52 weeks | |
| 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 statistical analyses for this end point | |

| End point values | Placebo | Evinacumab | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 10 | 11 | | |
| Units: Percentage | | | | |
| number (not applicable) | 10.0 | 27.3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in fasting triglycerides (TGs) - (from baseline to week 52)

| | |
|------------------------|--|
| End point title | Percent change in fasting triglycerides (TGs) - (from baseline to week 52) |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to week 52 | |

| End point values | Placebo | Evinacumab | | |
|-----------------------------|------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[2] | 1 | | |
| Units: Percent | | | | |
| number (not applicable) | | -92.88 | | |

Notes:

[2] - Early termination of study due to low feasibility

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Apolipoprotein C3 (ApoC3) from Baseline to Week 52

| | |
|-----------------|--|
| End point title | Percent Change in Apolipoprotein C3 (ApoC3) from Baseline to Week 52 |
|-----------------|--|

End point description:

Apolipoproteins transport lipids through the body by binding with fat and cholesterol to form lipoproteins. ApoC3 was a component of very-low-density lipoproteins (VLDL), high-density lipoprotein (HDL), and triglyceride-rich chylomicrons and regulates lipid metabolism. Percent change in ApoC3 from Baseline to Week 52 was reported.

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

End point timeframe:

Baseline to week 52

| End point values | Placebo | Evinacumab | | |
|-----------------------------|------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[3] | 1 | | |
| Units: Percent | | | | |
| number (not applicable) | | -73.78 | | |

Notes:

[3] - Early termination of study due to low feasibility

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in non-high-density lipoprotein cholesterol (non-HDL-C) - (from baseline to week 52)

| | |
|-----------------|---|
| End point title | Percent change in non-high-density lipoprotein cholesterol (non-HDL-C) - (from baseline to week 52) |
|-----------------|---|

End point description:

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

End point timeframe:

Baseline to week 52

| End point values | Placebo | Evinacumab | | |
|-----------------------------|------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[4] | 1 | | |
| Units: Percent | | | | |
| number (not applicable) | | -60.12 | | |

Notes:

[4] - Early termination of study due to low feasibility

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in Apolipoprotein B48 (ApoB48) from baseline to week 52

| | |
|------------------------|--|
| End point title | Percent change in Apolipoprotein B48 (ApoB48) from baseline to week 52 |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to week 52 | |

| End point values | Placebo | Evinacumab | | |
|-----------------------------|------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[5] | 1 | | |
| Units: Percent | | | | |
| number (not applicable) | | -92.09 | | |

Notes:

[5] - Early termination of study due to low feasibility

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in total cholesterol (TC) - (baseline to week 52)

| | |
|------------------------|--|
| End point title | Percent change in total cholesterol (TC) - (baseline to week 52) |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to week 52 | |

| End point values | Placebo | Evinacumab | | |
|-----------------------------|------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[6] | 1 | | |
| Units: Percent | | | | |
| number (not applicable) | | -57.62 | | |

Notes:

[6] - Early termination of study due to low feasibility

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in Apolipoprotein B100 (ApoB100) levels from baseline to week 52

| | |
|------------------------|---|
| End point title | Percent change in Apolipoprotein B100 (ApoB100) levels from baseline to week 52 |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to week 52 | |

| End point values | Placebo | Evinacumab | | |
|-----------------------------|------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[7] | 1 | | |
| Units: Percent | | | | |
| number (not applicable) | | 225.14 | | |

Notes:

[7] - Early termination of study due to low feasibility

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Nuclear Magnetic Resonance (NMR)-Determined Particle Size and Number From Baseline to Week 52

| | |
|------------------------|---|
| End point title | Percent Change in Nuclear Magnetic Resonance (NMR)-Determined Particle Size and Number From Baseline to Week 52 |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to week 52 | |

| End point values | Placebo | Evinacumab | | |
|--------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[8] | 0 ^[9] | | |
| Units: Percent | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[8] - Early termination of study due to low feasibility

[9] - Early termination of study due to low feasibility

Statistical analyses

No statistical analyses for this end point

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

| | |
|--|---|
| End point title | Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Serious TEAEs |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| From start of study drug administration up to off drug follow-up (up to Week 72) | |

| End point values | Placebo | Evinacumab | | |
|---------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 10 | 11 | | |
| Units: Participants | | | | |
| Participants with TEAEs | 10 | 7 | | |
| Participants with Serious TEAEs | 4 | 5 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Independently Adjudicated Positive Episodes of Acute Pancreatitis (AP) Per Participant

| | |
|------------------------|--|
| End point title | Number of Independently Adjudicated Positive Episodes of Acute Pancreatitis (AP) Per Participant |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Up to 52 weeks | |

| End point values | Placebo | Evinacumab | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 10 | 11 | | |
| Units: Number of Episodes | | | | |
| arithmetic mean (standard deviation) | 0.1 (\pm 0.32) | 0.4 (\pm 0.67) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With TEAEs Based on Severity

| | |
|-----------------|---|
| End point title | Number of Participants With TEAEs Based on Severity |
|-----------------|---|

End point description:

AE was defined any untoward medical occurrence in a participant administered with a study drug, which does not necessarily had a causal relationship with this treatment. TEAEs are defined as AEs that developed or worsened during the treatment period. Severity of TEAEs was graded according to the following scale: Mild: Does not interfere in a significant manner with the participants normal functioning level, Moderate: Produces some impairment of functioning but is not hazardous to health and Severe: Produces significant impairment of functioning or incapacitation and is a definite hazard to the participants health.

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

End point timeframe:

From start of study drug administration up to off drug follow-up (up to Week 72)

| End point values | Placebo | Evinacumab | | |
|----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 10 | 7 | | |
| Units: Participants | | | | |
| number (not applicable) | | | | |
| Participants with Mild TEAEs | 3 | 3 | | |
| Participants with Moderate TEAEs | 3 | 1 | | |
| Participants with Severe TEAEs | 4 | 3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Changes from Baseline in Laboratory Parameters

| | |
|-----------------|---|
| End point title | Number of Participants With Clinically Significant Changes from Baseline in Laboratory Parameters |
|-----------------|---|

End point description:

Clinical laboratory parameters included biochemistry, hematology and urinalysis. The number of participants with clinically significant changes from baseline in laboratory parameters were reported. Clinical significance was determined by the investigator.

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

End point timeframe:

From start of study drug administration up to off drug follow-up (up to Week 72)

| End point values | Placebo | Evinacumab | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 10 | 11 | | |
| Units: Participants | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive Treatment-emergent Anti-Drug Antibodies (ADA)

| | |
|-----------------|--|
| End point title | Number of Participants With Positive Treatment-emergent Anti-Drug Antibodies (ADA) |
|-----------------|--|

End point description:

Treatment-Emergent ADA was defined as any positive post baseline assay response when baseline results were negative or missing. Treatment-Emergent ADA responses were further classified as: Persistent (a positive result in the ADA assay detected in at least 2 consecutive post baseline samples separated by at least a 16-week post baseline period [based on] nominal sampling time], with no ADA-negative results in-between, regardless of any missing samples); Indeterminate (a positive result in the ADA assay at the last collection time point only, regardless of any missing samples); Transient (not persistent/indeterminate, regardless of any missing samples). Number of participants with positive treatment-emergent ADA response during Week 52 were reported.

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

End point timeframe:

Baseline to Week 52

| End point values | Placebo | Evinacumab | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 7 | | |
| Units: Participants | | | | |
| number (not applicable) | | | | |
| Persistent: Treatment-Emergent Response | 0 | 0 | | |
| Transient: Treatment-Emergent Response | 0 | 0 | | |
| Indeterminate: Treatment-Emergent Response | 0 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive Neutralizing Antibodies (NAb)

| | |
|-----------------|--|
| End point title | Number of Participants With Positive Neutralizing Antibodies (NAb) |
|-----------------|--|

End point description:

NAb positive was defined as presence of at least one positive nAb sample.

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

End point timeframe:

Baseline to Week 52

| End point values | Placebo | Evinacumab | | |
|-----------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[10] | 0 ^[11] | | |
| Units: Participants | | | | |

Notes:

[10] - Early termination of study due to low feasibility

[11] - Early termination of study due to low feasibility

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Fasting High-density Lipoprotein Cholesterol (HDL-C) From Baseline to Week 52

| | |
|-----------------|---|
| End point title | Percent Change in Fasting High-density Lipoprotein Cholesterol (HDL-C) From Baseline to Week 52 |
|-----------------|---|

End point description:

Percent Change in fasting HDL-C from Baseline to Week 52 was reported.

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

End point timeframe:

Baseline to Week 52

| End point values | Placebo | Evinacumab | | |
|-----------------------------|-------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[12] | 1 | | |
| Units: Percent change | | | | |
| number (not applicable) | | 52.94 | | |

Notes:

[12] - Early termination of study due to low feasibility

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of Total Evinacumab in Serum

| | |
|-----------------|--|
| End point title | Concentration of Total Evinacumab in Serum ^[13] |
|-----------------|--|

End point description:

Concentration of total evinacumab in serum by time at Pre-dose and End of Infusion were analyzed and reported.

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

End point timeframe:

Pre-dose and End of Infusion (EOI) at Weeks 0, 4, 8, 12, 16, 20, 24, 32, 36, 40, 44, and 48; Pre-dose at Weeks 28 and 52

Notes:

[13] - 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: No statistical analyses for this end point

| End point values | Evinacumab | | | |
|--------------------------------------|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 10 | | | |
| Units: milligrams per liter (mg/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0: Pre-dose | 1.39 (± 4.40) | | | |
| Week 0: EOI (End of Infusion) | 573 (± 95.7) | | | |
| Week 4: Pre-dose | 97.6 (± 37.4) | | | |
| Week 4: EOI (End of Infusion) | 638 (± 286) | | | |
| Week 8: Pre-dose | 133 (± 88.6) | | | |
| Week 8: EOI (End of Infusion) | 724 (± 123) | | | |
| Week 12: Pre-dose | 158 (± 81.1) | | | |
| Week 12: EOI (End of Infusion) | 749 (± 215) | | | |
| Week 16: Pre-dose | 201 (± 68.7) | | | |
| Week 16: EOI (End of Infusion) | 999.99 (± 999.99) | | | |
| Week 20: Pre-dose | 999.99 (± 999.99) | | | |
| Week 20: EOI (End of Infusion) | 999.99 (± 999.99) | | | |
| Week 24: Pre-dose | 999.99 (± 999.99) | | | |
| Week 24: EOI (End of Infusion) | 999.99 (± 999.99) | | | |
| Week 28: Pre-dose | 999.99 (± 999.99) | | | |

| | | | | |
|--------------------------------|-------------------|--|--|--|
| Week 32: Pre-dose | 999.99 (± 999.99) | | | |
| Week 32: EOI (End of Infusion) | 999.99 (± 999.99) | | | |
| Week 36: Pre-dose | 99.1 (± 171) | | | |
| Week 36: EOI (End of Infusion) | 999.99 (± 999.99) | | | |
| Week 40: Pre-dose | 999.99 (± 999.99) | | | |
| Week 40: EOI (End of Infusion) | 999.99 (± 999.99) | | | |
| Week 44: Pre-dose | 999.99 (± 999.99) | | | |
| Week 44: EOI (End of Infusion) | 999.99 (± 999.99) | | | |
| Week 48: Pre-dose | 999.99 (± 999.99) | | | |
| Week 48: EOI (End of Infusion) | 999.99 (± 999.99) | | | |
| Week 52: Pre-dose | 999.99 (± 999.99) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Fasting Low Density Lipoprotein (LDL-C) From Baseline to Week 52

| | |
|---|--|
| End point title | Percent Change in Fasting Low Density Lipoprotein (LDL-C) From Baseline to Week 52 |
| End point description: LDL-C levels were determined in beta-quantification with ultracentrifugation method. Percent change in fasting LDL-C from Baseline to Week 52 was reported. | |
| End point type | Secondary |
| End point timeframe: Baseline to Week 52 | |

| End point values | Placebo | Evinacumab | | |
|-----------------------------|-------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[14] | 1 | | |
| Units: Percent | | | | |
| number (not applicable) | | 695.00 | | |

Notes:

[14] - Early termination of study due to low feasibility

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of Total Angiopoietin-like 3 (ANGPTL3) in Serum

| | |
|---|---|
| End point title | Concentration of Total Angiopoietin-like 3 (ANGPTL3) in |
| End point description: Concentration of total ANGPTL3 in serum by time were analyzed and reported. | |
| End point type | Secondary |
| End point timeframe: Pre-dose and End of Infusion (EOI) at Weeks 0, 4, 8, 12, 16, 20, 24, 32, 36, 40, 44, and 48; Pre-dose at Weeks 28 and 52 | |
| Notes: [15] - 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: No statistical analyses for this end point | |

| End point values | Evinacumab | | | |
|--------------------------------------|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 10 | | | |
| Units: mg/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0: Pre-Dose | 0.0907 (± 0.0272) | | | |
| Week 0: EOI (End of Infusion) | 0.211 (± 0.0362) | | | |
| Week 4: Pre-Dose | 0.248 (± 0.105) | | | |
| Week 4: EOI (End of Infusion) | 0.306 (± 0.0992) | | | |
| Week 8: Pre-Dose | 0.243 (± 0.0811) | | | |
| Week 8: EOI (End of Infusion) | 0.298 (± 0.0831) | | | |
| Week 12: Pre-Dose | 0.281 (± 0.0851) | | | |
| Week 12: EOI (End of Infusion) | 0.322 (± 0.0672) | | | |
| Week 16: Pre-Dose | 0.230 (± 0.0560) | | | |
| Week 16: EOI (End of Infusion) | 999.99 (± 999.99) | | | |
| Week 20: Pre-Dose | 999.99 (± 999.99) | | | |
| Week 20: EOI (End of Infusion) | 999.99 (± 999.99) | | | |
| Week 24: Pre-Dose | 999.99 (± 999.99) | | | |
| Week 24: EOI (End of Infusion) | 999.99 (± 999.99) | | | |
| Week 28: Pre-Dose | 999.99 (± 999.99) | | | |
| Week 32: Pre-Dose | 999.99 (± 999.99) | | | |
| Week 32: EOI (End of Infusion) | 999.99 (± 999.99) | | | |
| Week 36: Pre-Dose | 0.162 (± 0.107) | | | |
| Week 36: EOI (End of Infusion) | 999.99 (± 999.99) | | | |
| Week 40: Pre-Dose | 999.99 (± 999.99) | | | |

| | | | | |
|--------------------------------|-------------------|--|--|--|
| Week 40: EOI (End of Infusion) | 999.99 (± 999.99) | | | |
| Week 44: Pre-Dose | 999.99 (± 999.99) | | | |
| Week 44: EOI (End of Infusion) | 999.99 (± 999.99) | | | |
| Week 48: Pre-Dose | 999.99 (± 999.99) | | | |
| Week 48: EOI (End of Infusion) | 999.99 (± 999.99) | | | |
| Week 52: Pre-Dose | 999.99 (± 999.99) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study drug administration up to off drug follow-up (72 weeks)

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | Evinacumab 20 mg |
|-----------------------|------------------|

Reporting group description:

Participants received evinacumab 20 mg/kg IV infusion Q4W starting from Day 1 up to 52 weeks.

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Randomized 1:1

| Serious adverse events | Evinacumab 20 mg | Placebo | |
|--|------------------|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 11 (45.45%) | 4 / 10 (40.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 1 / 10 (10.00%) | |
| occurrences causally related to treatment / all | 3 / 3 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 2 / 10 (20.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Evinacumab 20 mg | Placebo | |
|--|-------------------------|-----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 11 (72.73%) | 8 / 10 (80.00%) | |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| General disorders and administration site conditions | | | |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|---|---|--|--|
| Fatigue subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 | |
| Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | |
| Investigations Pedal pulse decreased subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | |
| Injury, poisoning and procedural complications Epicondylitis subjects affected / exposed occurrences (all) Limb injury subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | |
| Gastrointestinal disorders | | | |

| | | | |
|--|-----------------|-----------------|--|
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 2 / 10 (20.00%) | |
| occurrences (all) | 0 | 2 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pancreatic pseudocyst | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 2 / 10 (20.00%) | |
| occurrences (all) | 1 | 2 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Duodenitis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 4 / 11 (36.36%) | 3 / 10 (30.00%) | |
| occurrences (all) | 5 | 6 | |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Urticaria | | | |

| | | | |
|---|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 3 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 | |
| Infections and infestations Influenza subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 | |
| Hand-foot-and-mouth disease subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 | |
| Wound infection subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 2 | 0 / 10 (0.00%) 0 | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | |
| Cellulitis subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | |
| Bronchitis subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | |
| COVID-19 subjects affected / exposed occurrences (all) | 3 / 11 (27.27%) 3 | 1 / 10 (10.00%) 1 | |
| Metabolism and nutrition disorders Food intolerance subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 | |
| Hypoglycaemia subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|----------------------|
| 16 December 2021 | Protocol Amendment 2 |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|------------------|-------------------|--------------|
| 15 February 2023 | Study Termination | - |

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

| |
|--|
| The sponsor terminated the study early due to enrollment issues. |
|--|

Notes: