



Clinical trial results:

Phase III, single-arm, open-label, international, multi-centre study to evaluate the efficacy and safety of lomitapide in paediatric patients with Homozygous Familial Hypercholesterolaemia (HoFH) on stable lipid-lowering therapy

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2019-002278-30 |
| Trial protocol | DE IT |
| Global end of trial date | 06 June 2024 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 21 December 2024 |
| First version publication date | 21 December 2024 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | APH-19 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04681170 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Amryt Pharmaceuticals DAC |
| Sponsor organisation address | 45 Mespil Road, Dublin 4, Ireland, |
| Public contact | Head of Clinical Operations, Amryt Pharmaceuticals DAC, 353 15180200, janet.boylan@amrytpharma.com |
| Scientific contact | Head of Clinical Operations, Amryt Pharmaceuticals DAC, 353 15180200, janet.boylan@amrytpharma.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-001124-PIP01-10 |
| 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? | Yes |

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 02 July 2024 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 06 June 2024 |
| Global end of trial reached? | Yes |
| Global end of trial date | 06 June 2024 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of lomitapide as defined by the percent change in low-density lipoprotein cholesterol (LDL-C) at the maximum tolerated dose (MTD) at Week 24±3 days (W24) compared to baseline when added to stable lipid-lowering therapy (LLT, including lipoprotein apheresis [LA] where applicable) in paediatric patients (5 to ≤17 years of age) with HoFH.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and with Good Clinical Practice (GCP) guidelines as denoted in the International Conference on Harmonization (ICH) E6 requirements. These practices included IRB/IEC procedures, informed consent, protocol adherence, administrative documents, drug supply accountability, data collection, patient records (source documents), adverse event (AE) recording and reporting, inspection and audit preparation, and record retention. The Investigator was made aware that regulatory authorities and representatives of the Sponsor could inspect the documents and patient records at any time. All subject identities were kept confidential. Each subject was assigned a unique subject number, which in turn was used in the electronic case report form (eCRF) instead of the subject's name.

Background therapy:

All subjects were required to complete a Run in Period of a minimum of 6 weeks. During the Run in period, subjects were stabilised on their current LLT (including LA, if applicable). Each subject was to remain on their stable LLT regimen (including LA, if applicable) during the 24 week Efficacy Phase. After 24 weeks, adjustments to background LLT (including LA, if applicable) were allowed for optimal standard of care at the discretion of the Investigator.

Evidence for comparator:

Not applicable

| | |
|---|------------------|
| Actual start date of recruitment | 14 December 2020 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | Saudi Arabia: 15 |
| Country: Number of subjects enrolled | Tunisia: 7 |
| Country: Number of subjects enrolled | Israel: 3 |
| Country: Number of subjects enrolled | Spain: 7 |
| Country: Number of subjects enrolled | Germany: 7 |
| Country: Number of subjects enrolled | Italy: 7 |
| Worldwide total number of subjects | 46 |
| EEA total number of subjects | 21 |

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) | 21 |
| Adolescents (12-17 years) | 25 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Male and female subjects aged 5 to ≤ 17 years with HoFH were enrolled in the trial at 12 study centres in various countries (3 in Germany, 1 in Israel, 2 in Italy, 2 in Saudi Arabia, 3 in Spain and 1 in Tunisia). The first patient first visit was 14 Dec 2020 and the last patient last visit was 06 Jun 2024.

Pre-assignment

Screening details:

Subjects underwent assessments to determine eligibility at the Initial Screening Visit (up to 12 weeks prior to Day 0).

A total of 46 subjects were enrolled in this study. Of these, 3 subjects were 'Run in' failures and did not complete the Run in Period.). Therefore, a total of 43 (93.5%) subjects entered the Efficacy Phase at Visit 4.

Period 1

| | |
|------------------------------|----------------|
| Period 1 title | Pre-run in |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|--|---|
| Arm title | All patients from all age groups |
| Arm description: - | |
| Arm type | Main arm - screening phase - no IMP administrated |
| Investigational medicinal product name | Lomitapide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

In the screening phase no IMP has been administered.

| | |
|--------------------------------|----------------------------------|
| Number of subjects in period 1 | All patients from all age groups |
| Started | 46 |
| Completed | 46 |

Period 2

| | |
|------------------------------|-------------------------------|
| Period 2 title | Stratified enrolment & run-in |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|---|-----------------|
| Arm title | All age groups |
| Arm description: - | |
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 2 | All age groups |
|--|----------------|
| Started | 46 |
| Completed | 43 |
| Not completed | 3 |
| Consent withdrawn by subject | 1 |
| Death due to a non-treatment emergent AE | 1 |
| Protocol deviation | 1 |

Period 3

| | |
|------------------------------|---------------------------|
| Period 3 title | Open label efficacy phase |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|------------|
| Are arms mutually exclusive? | No |
| Arm title | 5-10 years |

| | |
|--|---------------|
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Lomitapide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Lomitapide capsules were provided in 4 dose strengths of 2 mg, 5 mg, 10 mg, and 20 mg and were administered orally once daily.

After stabilization of each subject on his/her current MTD of LLT (including LA, if applicable) during the 6 week Run in Period, treatment with lomitapide was started as add on therapy on Day 0 of the Efficacy Phase.

The dose was initiated at the recommended starting dose for the subject's age and escalated to the maximum dose applicable to their age as shown below based upon safety and tolerability in addition to LDL C values:

- 5-10 years old subjects: Starting dose 2 mg/day; MTD 20 mg/day

| | |
|-----------|-------------|
| Arm title | 11-17 years |
|-----------|-------------|

| | |
|--|---------------|
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Lomitapide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Lomitapide capsules were provided in 4 dose strengths of 2 mg, 5 mg, 10 mg, and 20 mg and were administered orally once daily.

After stabilization of each subject on his/her current MTD of LLT (including LA, if applicable) during the 6 week Run in Period, treatment with lomitapide was started as add on therapy on Day 0 of the Efficacy Phase.

The dose was initiated at the recommended starting dose for the subject's age and escalated to the maximum dose applicable to their age as shown below based upon safety and tolerability in addition to LDL C values:

- 11-15 years old subjects: Starting dose 2 mg/day; MTD 40 mg/day
- 16-17 years old subjects: Starting dose 5 mg/day; MTD 60 mg/day

| | |
|--|----------------|
| Arm title | All age groups |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Lomitapide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Lomitapide capsules were provided in 4 dose strengths of 2 mg, 5 mg, 10 mg, and 20 mg and were administered orally once daily.

After stabilization of each subject on his/her current MTD of LLT (including LA, if applicable) during the 6 week Run in Period, treatment with lomitapide was started as add on therapy on Day 0 of the Efficacy Phase.

The dose was initiated at the recommended starting dose for the subject's age and escalated to the maximum dose applicable to their age as shown below based upon safety and tolerability in addition to LDL C values:

- 5-10 years old subjects: Starting dose 2 mg/day; MTD 20 mg/day
- 11-15 years old subjects: Starting dose 2 mg/day; MTD 40 mg/day
- 16-17 years old subjects: Starting dose 5 mg/day; MTD 60 mg/day

| Number of subjects in period 3 | 5-10 years | 11-17 years | All age groups |
|---------------------------------------|------------|-------------|----------------|
| Started | 20 | 23 | 43 |
| Completed | 20 | 21 | 41 |
| Not completed | 0 | 2 | 2 |
| Adverse event, non-fatal | - | 2 | 2 |

Period 4

| | |
|------------------------------|-------------------------|
| Period 4 title | Open label safety phase |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|----------------|
| Are arms mutually exclusive? | Yes |
| Arm title | All age groups |

Arm description: -

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Lomitapide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Each subject was to continue to receive their MTD of lomitapide achieved during the Efficacy Phase (unless criteria were met for reducing or increasing the dose) for an additional 80±1 weeks in the Safety Phase (for a total treatment period of 2 years).

| | |
|------------------|------------|
| Arm title | 5-10 years |
|------------------|------------|

Arm description: -

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Lomitapide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Each subject was to continue to receive their MTD of lomitapide achieved during the Efficacy Phase (unless criteria were met for reducing or increasing the dose) for an additional 80±1 weeks in the Safety Phase (for a total treatment period of 2 years).

| | |
|------------------|-------------|
| Arm title | 11-17 years |
|------------------|-------------|

Arm description: -

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Lomitapide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Each subject was to continue to receive their MTD of lomitapide achieved during the Efficacy Phase (unless criteria were met for reducing or increasing the dose) for an additional 80±1 weeks in the Safety Phase (for a total treatment period of 2 years).

| Number of subjects in period 4 | All age groups | 5-10 years | 11-17 years |
|---------------------------------------|----------------|------------|-------------|
| Started | 41 | 20 | 21 |
| Completed | 39 | 20 | 19 |
| Not completed | 2 | 0 | 2 |
| Consent withdrawn by subject | 1 | - | 1 |
| AEs and none compliance | 1 | - | 1 |

Baseline characteristics

Reporting groups

Reporting group title

Pre-run in

Reporting group description: -

| Reporting group values | Pre-run in | Total | |
|------------------------|------------|-------|--|
| Number of subjects | 46 | 46 | |
| Age categorical | | | |
| Units: Subjects | | | |
| 5-10 years | 21 | 21 | |
| 11-17 years | 25 | 25 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 25 | 25 | |
| Male | 21 | 21 | |

End points

End points reporting groups

| | |
|--------------------------------|----------------------------------|
| Reporting group title | All patients from all age groups |
| Reporting group description: - | |
| Reporting group title | All age groups |
| Reporting group description: - | |
| Reporting group title | 5-10 years |
| Reporting group description: - | |
| Reporting group title | 11-17 years |
| Reporting group description: - | |
| Reporting group title | All age groups |
| Reporting group description: - | |
| Reporting group title | All age groups |
| Reporting group description: - | |
| Reporting group title | 5-10 years |
| Reporting group description: - | |
| Reporting group title | 11-17 years |
| Reporting group description: - | |

Primary: LDL-C at Baseline and Week 24/LOCF

| | |
|--|---|
| End point title | LDL-C at Baseline and Week 24/LOCF ^[1] |
| End point description: | |
| | |
| End point type | Primary |
| End point timeframe: | |
| Percent change from Baseline in LDL-C at Week 24±3 days. | |

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: This was a single-arm study, no comparative group can be assigned; the comparison made is done only between baseline and Week 24. Analysis was made using the one-sample t-test to test the null hypothesis that the percentage change from Baseline was equal to zero against the alternative hypothesis that the percentage change from Baseline was not equal to zero.

| End point values | All age groups | | | |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 435.791 (± 189.4620) | | | |
| Week 24/LOCF | 175.404 (± 89.8979) | | | |
| Change from Baseline | -260.386 (± 192.1284) | | | |
| Percent Change from Baseline | -53.910 (± 25.8287) | | | |

| | |
|-----------------------------------|--|
| Attachments (see zip file) | Waterfall Plot of Percentage Change from Baseline/Waterfall. |
|-----------------------------------|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in non-HDL-C from Baseline at Week 24/LOCF

| | |
|---|---|
| End point title | Percent Change in non-HDL-C from Baseline at Week 24/LOCF |
| End point description: Analysis was made using the one-sample t-test to test the null hypothesis that the percentage change from Baseline was equal to zero against the alternative hypothesis that the percentage change from Baseline was not equal to zero. | |
| End point type | Secondary |
| End point timeframe: Percent change from Baseline at Week 24±3 days for the lipid parameter non-HDL-C | |

| End point values | All age groups | | | |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Observed Value | 183.632 (± 92.0566) | | | |
| Change from Baseline | -270.493 (± 194.7326) | | | |
| Percent Change from Baseline | -54.185 (± 25.0256) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in TC from Baseline at Week 24/LOCF

| | |
|---|--|
| End point title | Percent Change in TC from Baseline at Week 24/LOCF |
| End point description: Analysis was made using the one-sample t-test to test the null hypothesis that the percentage change from Baseline was equal to zero against the alternative hypothesis that the percentage change from Baseline was not equal to zero. | |
| End point type | Secondary |
| End point timeframe: Percent change from Baseline at Week 24±3 days for the lipid parameter TC | |

| | | | | |
|--------------------------------------|----------------------------|--|--|--|
| End point values | All age groups | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Observed Value | 216.866 (\pm 94.1528) | | | |
| Change from Baseline | -268.668 (\pm 194.2576) | | | |
| Percent Change from Baseline | -50.176 (\pm 24.5397) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in VLDL-C from Baseline at Week 24/LOCF

| | |
|---|--|
| End point title | Percent Change in VLDL-C from Baseline at Week 24/LOCF |
| End point description: | |
| Analysis was made using the one-sample t-test to test the null hypothesis that the percentage change from Baseline was equal to zero against the alternative hypothesis that the percentage change from Baseline was not equal to zero. | |
| End point type | Secondary |
| End point timeframe: | |
| Percent change from Baseline at Week 24 \pm 3 days for the lipid parameter VLDL-C | |

| | | | | |
|--------------------------------------|--------------------------|--|--|--|
| End point values | All age groups | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Observed Value | 8.344 (\pm 4.7206) | | | |
| Change from Baseline | -9.981 (\pm 8.1272) | | | |
| Percent Change from Baseline | -49.678 (\pm 31.6126) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Apo B from Baseline at Week 24/LOCF

| | |
|-----------------|---|
| End point title | Percent Change in Apo B from Baseline at Week 24/LOCF |
|-----------------|---|

End point description:

Analysis was made using the one-sample t-test to test the null hypothesis that the percentage change from Baseline was equal to zero against the alternative hypothesis that the percentage change from Baseline was not equal to zero.

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

End point timeframe:

Percent change from Baseline at Week 24±3 days for the lipid parameter Apo B

| End point values | All age groups | | | |
|--------------------------------------|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Observed Value | 131.3 (± 62.59) | | | |
| Change from Baseline | -185.3 (± 130.66) | | | |
| Percent Change from Baseline | -53.1 (± 24.76) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Triglycerides from Baseline at Week 24/LOCF

| | |
|-----------------|---|
| End point title | Percent Change in Triglycerides from Baseline at Week 24/LOCF |
|-----------------|---|

End point description:

Analysis was made using the one-sample t-test to test the null hypothesis that the percentage change from Baseline was equal to zero against the alternative hypothesis that the percentage change from Baseline was not equal to zero.

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

End point timeframe:

Percent change from Baseline at Week 24±3 days for the lipid parameter Triglycerides

| End point values | All age groups | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Observed Value | 42.068 (± 23.1235) | | | |
| Change from Baseline | -49.828 (± 40.4354) | | | |

| | | | | |
|------------------------------|--------------------|--|--|--|
| Percent Change from Baseline | -49.28 (± 31.7290) | | | |
|------------------------------|--------------------|--|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Lipid Parameter Lp(a) from Baseline at Week 24/LOCF

| | |
|-----------------|---|
| End point title | Percent Change in Lipid Parameter Lp(a) from Baseline at Week 24/LOCF |
|-----------------|---|

End point description:

Analysis was made using the one-sample t-test to test the null hypothesis that the percentage change from Baseline was equal to zero against the alternative hypothesis that the percentage change from Baseline was not equal to zero.

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

End point timeframe:

Percent change from Baseline at Week 24±3 days for the lipid parameter Lp(a)

| | | | | |
|--------------------------------------|---------------------|--|--|--|
| End point values | All age groups | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 28 | | | |
| Units: nmol/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| Observed Value | 82.493 (± 75.5080) | | | |
| Change from Baseline | -47.383 (± 59.2811) | | | |
| Percent Change from Baseline | -26.757 (± 32.5675) | | | |

| | |
|-----------------------------------|--|
| Attachments (see zip file) | Change in Lp(a) (mg/dL vs. nmol/L)/Lp(a).pdf |
|-----------------------------------|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in LDL-C from Baseline at All Other Time Points to Week 104 (efficacy phase results from Baseline to Week 24)

| | |
|-----------------|--|
| End point title | Percent Change in LDL-C from Baseline at All Other Time Points to Week 104 (efficacy phase results from Baseline to Week 24) |
|-----------------|--|

End point description:

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

End point timeframe:

From Baseline at All Other Time Points to Week 104 (refer also to the below-listed results covering the safety phase)

| End point values | All age groups | | | |
|--------------------------------------|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 | -1.962 (\pm 20.7168) | | | |
| Week 8 | -6.798 (\pm 19.1524) | | | |
| Week 12 | -16.638 (\pm 23.1978) | | | |
| Week 16 | -36.458 (\pm 17.9894) | | | |
| Week 20 | -50.730 (\pm 24.8321) | | | |
| Week 24 | -54.602 (\pm 26.4557) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in LDL-C from Baseline at All Other Time Points to Week 104 (safety phase results from Week 28 to Week 104)

| | |
|-----------------|--|
| End point title | Percent Change in LDL-C from Baseline at All Other Time Points to Week 104 (safety phase results from Week 28 to Week 104) |
|-----------------|--|

End point description:

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

End point timeframe:

From Baseline at All Other Time Points to Week 104 (refer also to the above-listed results covering the efficacy phase)

| End point values | All age groups | | | |
|--------------------------------------|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 28 | -55.518 (\pm 28.5714) | | | |
| Week 32 | -52.126 (\pm 28.7496) | | | |

| | | | | |
|----------|---------------------|--|--|--|
| Week 36 | -39.823 (± 32.6612) | | | |
| Week 40 | -49.427 (± 29.5830) | | | |
| Week 44 | -44.312 (± 30.3775) | | | |
| Week 48 | -45.315 (± 29.6526) | | | |
| Week 52 | -44.583 (± 32.8128) | | | |
| Week 56 | -45.994 (± 34.3631) | | | |
| Week 68 | -40.831 (± 37.3821) | | | |
| Week 80 | -42.319 (± 34.9400) | | | |
| Week 92 | -37.199 (± 39.6625) | | | |
| Week 104 | -40.159 (± 30.5026) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in non-HDL-C from Baseline at All Other Time Points to Week 104 (efficacy phase results from Baseline to Week 24)

| | |
|-----------------|--|
| End point title | Percent Change in non-HDL-C from Baseline at All Other Time Points to Week 104 (efficacy phase results from Baseline to Week 24) |
|-----------------|--|

End point description:

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

End point timeframe:

Percent Change in non-HDL-C from Baseline at All Other Time Points to Week 104 (refer also to the below-listed results covering the safety phase)

| End point values | All age groups | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 | -1.765 (± 21.1682) | | | |
| Week 8 | -6.745 (± 18.6776) | | | |
| Week 12 | -16.497 (± 22.9850) | | | |
| Week 16 | -36.610 (± 17.4339) | | | |

| | | | | |
|---------|---------------------|--|--|--|
| Week 20 | -50.928 (± 24.3958) | | | |
| Week 24 | -55.033 (± 25.4297) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in non-HDL-C from Baseline at All Other Time Points to Week 104 (safety phase results from Week 28 to Week 104)

| | |
|-----------------|--|
| End point title | Percent Change in non-HDL-C from Baseline at All Other Time Points to Week 104 (safety phase results from Week 28 to Week 104) |
|-----------------|--|

End point description:

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

End point timeframe:

Percent Change in non-HDL-C from Baseline at All Other Time Points to Week 104 (refer also to the below-listed results covering the efficacy phase)

| End point values | All age groups | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 28 | -55.984 (± 27.5559) | | | |
| Week 32 | -52.629 (± 27.8748) | | | |
| Week 36 | -40.574 (± 31.4293) | | | |
| Week 40 | -50.013 (± 28.4878) | | | |
| Week 44 | -44.702 (± 29.8885) | | | |
| Week 48 | -46.770 (± 29.3974) | | | |
| Week 52 | -45.222 (± 31.9577) | | | |
| Week 56 | -46.558 (± 33.4734) | | | |
| Week 68 | -41.576 (± 36.0854) | | | |
| Week 80 | -42.388 (± 34.3439) | | | |
| Week 92 | -37.755 (± 38.4243) | | | |
| Week 104 | -40.511 (± 30.1102) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in TC from Baseline at All Other Time Points to Week 104 (efficacy phase results from Baseline to Week 24)

| | |
|-----------------|---|
| End point title | Percent Change in TC from Baseline at All Other Time Points to Week 104 (efficacy phase results from Baseline to Week 24) |
|-----------------|---|

End point description:

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

End point timeframe:

Percent Change in TC from Baseline at All Other Time Points to Week 104 (refer also to the below-listed results covering the safety phase)

| End point values | All age groups | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 | -2.057 (± 19.3772) | | | |
| Week 8 | -6.970 (± 17.6904) | | | |
| Week 12 | -15.961 (± 21.4313) | | | |
| Week 16 | -33.976 (± 15.7159) | | | |
| Week 20 | -48.177 (± 23.2987) | | | |
| Week 24 | -50.922 (± 24.9738) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in TC from Baseline at All Other Time Points to Week 104 (safety phase results from Week 28 to Week 104)

| | |
|-----------------|---|
| End point title | Percent Change in TC from Baseline at All Other Time Points to Week 104 (safety phase results from Week 28 to Week 104) |
|-----------------|---|

End point description:

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

End point timeframe:

Percent Change in TC from Baseline at All Other Time Points to Week 104 (refer also to the above-listed results covering the efficacy phase)

| End point values | All age groups | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 28 | -51.998 (± 26.9668) | | | |
| Week 32 | -48.945 (± 26.2375) | | | |
| Week 36 | -40.643 (± 30.5125) | | | |
| Week 40 | -45.402 (± 27.5358) | | | |
| Week 44 | -41.443 (± 28.3745) | | | |
| Week 48 | -44.164 (± 27.6987) | | | |
| Week 52 | -42.764 (± 30.6617) | | | |
| Week 56 | -43.234 (± 31.3599) | | | |
| Week 68 | -39.672 (± 33.2025) | | | |
| Week 80 | -40.291 (± 31.9119) | | | |
| Week 92 | -34.946 (± 35.8485) | | | |
| Week 104 | -36.017 (± 32.2354) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in VLDL-C from Baseline at All Other Time Points to Week 104 (efficacy phase results from Baseline to Week 24)

| | |
|-----------------|---|
| End point title | Percent Change in VLDL-C from Baseline at All Other Time Points to Week 104 (efficacy phase results from Baseline to Week 24) |
|-----------------|---|

End point description:

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

End point timeframe:

Percent Change in VLDL-C from Baseline at All Other Time Points to Week 104 (refer also to the below-

| | | | | |
|--------------------------------------|--------------------------|--|--|--|
| End point values | All age groups | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 | 9.770 (\pm 42.2029) | | | |
| Week 8 | 2.857 (\pm 34.5887) | | | |
| Week 12 | -7.405 (\pm 48.8428) | | | |
| Week 16 | -34.706 (\pm 31.6590) | | | |
| Week 20 | -49.068 (\pm 25.6958) | | | |
| Week 24 | -53.050 (\pm 27.2118) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in VLDL-C from Baseline at All Other Time Points to Week 104 (safety phase results from Week 28 to Week 104)

| | |
|-----------------|---|
| End point title | Percent Change in VLDL-C from Baseline at All Other Time Points to Week 104 (safety phase results from Week 28 to Week 104) |
|-----------------|---|

End point description:

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

End point timeframe:

Percent Change in VLDL-C from Baseline at All Other Time Points to Week 104 (refer also to the above-listed results covering the efficacy phase)

| | | | | |
|--------------------------------------|--------------------------|--|--|--|
| End point values | All age groups | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 28 | -55.394 (\pm 25.0601) | | | |
| Week 32 | -47.899 (\pm 55.7396) | | | |

| | | | | |
|----------|---------------------|--|--|--|
| Week 36 | -46.596 (± 25.9994) | | | |
| Week 40 | -51.167 (± 26.7498) | | | |
| Week 44 | -46.750 (± 33.3163) | | | |
| Week 48 | -38.148 (± 50.6100) | | | |
| Week 52 | -49.469 (± 30.0996) | | | |
| Week 56 | -47.051 (± 32.7429) | | | |
| Week 68 | -47.832 (± 30.6844) | | | |
| Week 80 | -36.881 (± 44.5589) | | | |
| Week 92 | -41.368 (± 31.7375) | | | |
| Week 104 | -39.055 (± 40.2422) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in apo B from Baseline at All Other Time Points to Week 104 (efficacy phase results from Baseline to Week 24)

| | |
|-----------------|--|
| End point title | Percent Change in apo B from Baseline at All Other Time Points to Week 104 (efficacy phase results from Baseline to Week 24) |
|-----------------|--|

End point description:

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

End point timeframe:

Percent Change in apo B from Baseline at All Other Time Points to Week 104 (refer also to the below-listed results covering the safety phase)

| End point values | All age groups | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 | 0.2 (± 18.99) | | | |
| Week 8 | -6.5 (± 19.25) | | | |
| Week 12 | -15.5 (± 21.91) | | | |
| Week 16 | -36.1 (± 16.70) | | | |
| Week 20 | -51.6 (± 24.21) | | | |
| Week 24 | -54.0 (± 25.02) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in apo B from Baseline at All Other Time Points to Week 104 (safety phase results from Week 28 to Week 104)

| | |
|-----------------|--|
| End point title | Percent Change in apo B from Baseline at All Other Time Points to Week 104 (safety phase results from Week 28 to Week 104) |
|-----------------|--|

End point description:

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

End point timeframe:

Percent Change in apo B from Baseline at All Other Time Points to Week 104 (refer also to the above-listed results covering the efficacy phase)

| End point values | All age groups | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 28 | -56.2 (± 26.17) | | | |
| Week 32 | -52.0 (± 28.64) | | | |
| Week 36 | -43.9 (± 30.91) | | | |
| Week 40 | -48.9 (± 29.11) | | | |
| Week 44 | -46.1 (± 28.75) | | | |
| Week 48 | -48.6 (± 29.03) | | | |
| Week 52 | -47.7 (± 30.16) | | | |
| Week 56 | -47.1 (± 33.06) | | | |
| Week 68 | -44.8 (± 33.99) | | | |
| Week 80 | -47.1 (± 30.58) | | | |
| Week 92 | -41.8 (± 35.12) | | | |
| Week 104 | -44.6 (± 30.22) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in triglycerides from Baseline at All Other Time Points to Week 104 (efficacy phase results from Baseline to Week 24)

| | |
|-----------------|--|
| End point title | Percent Change in triglycerides from Baseline at All Other Time Points to Week 104 (efficacy phase results from Baseline to Week 24) |
|-----------------|--|

End point description:

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

End point timeframe:

Percent Change in triglycerides from Baseline at All Other Time Points to Week 104 (refer also to the below-listed results covering the safety phase)

| End point values | All age groups | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 | 9.387 (± 41.7233) | | | |
| Week 8 | 2.649 (± 35.3115) | | | |
| Week 12 | -7.258 (± 49.6990) | | | |
| Week 16 | -34.970 (± 30.2259) | | | |
| Week 20 | -48.989 (± 25.8872) | | | |
| Week 24 | -52.878 (± 26.8475) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in triglycerides from Baseline at All Other Time Points to Week 104 (safety phase results from Week 28 to Week 104)

| | |
|-----------------|--|
| End point title | Percent Change in triglycerides from Baseline at All Other Time Points to Week 104 (safety phase results from Week 28 to Week 104) |
|-----------------|--|

End point description:

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

End point timeframe:

Percent Change in triglycerides from Baseline at All Other Time Points to Week 104 (refer also to the above-listed results covering the efficacy phase)

| End point values | All age groups | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 28 | -55.639 (± 24.6317) | | | |
| Week 32 | -48.697 (± 54.0396) | | | |
| Week 36 | -46.823 (± 25.4762) | | | |
| Week 40 | -51.612 (± 25.9533) | | | |
| Week 44 | -47.065 (± 31.7596) | | | |
| Week 48 | -39.769 (± 48.3307) | | | |
| Week 52 | -49.415 (± 28.4096) | | | |
| Week 56 | -47.707 (± 32.0150) | | | |
| Week 68 | -48.471 (± 30.8061) | | | |
| Week 80 | -38.312 (± 44.1074) | | | |
| Week 92 | -41.549 (± 30.2027) | | | |
| Week 104 | -39.739 (± 39.8597) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in LP(a) from Baseline at All Other Time Points to Week 104 (efficacy phase results from Baseline to Week 24)

| | |
|-----------------|--|
| End point title | Percent Change in LP(a) from Baseline at All Other Time Points to Week 104 (efficacy phase results from Baseline to Week 24) |
|-----------------|--|

End point description:

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

End point timeframe:

Percent Change in LP(a) from Baseline at All Other Time Points to Week 104 (refer also to the below-listed results covering the safety phase)

| | | | | |
|--------------------------------------|---------------------|--|--|--|
| End point values | All age groups | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 28 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 | 9.660 (± 63.5768) | | | |
| Week 8 | 1.508 (± 46.1156) | | | |
| Week 12 | 0.592 (± 32.5241) | | | |
| Week 16 | -14.648 (± 26.3140) | | | |
| Week 20 | -16.602 (± 47.9856) | | | |
| Week 24 | -28.874 (± 33.5277) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in LP(a) from Baseline at All Other Time Points to Week 104 (safety phase results from Week 28 to Week 104)

| | |
|-----------------|--|
| End point title | Percent Change in LP(a) from Baseline at All Other Time Points to Week 104 (safety phase results from Week 28 to Week 104) |
|-----------------|--|

End point description:

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

End point timeframe:

Percent Change in LP(a) from Baseline at All Other Time Points to Week 104 (refer also to the above-listed results covering the efficacy phase)

| | | | | |
|--------------------------------------|---------------------|--|--|--|
| End point values | All age groups | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 28 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 28 | -32.628 (± 32.4047) | | | |
| Week 32 | -20.594 (± 50.1160) | | | |
| Week 36 | -25.278 (± 32.4201) | | | |
| Week 40 | -28.257 (± 34.6849) | | | |

| | | | | |
|----------|---------------------|--|--|--|
| Week 44 | -30.124 (± 34.9943) | | | |
| Week 48 | -17.905 (± 38.3429) | | | |
| Week 52 | -25.635 (± 42.3832) | | | |
| Week 56 | -22.366 (± 34.5809) | | | |
| Week 68 | -20.634 (± 42.9257) | | | |
| Week 80 | -22.659 (± 42.2271) | | | |
| Week 92 | -22.235 (± 41.1508) | | | |
| Week 104 | -29.064 (± 34.5930) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in TC/HDL-C ratio from Baseline at All Other Time Points to Week 104 (efficacy phase results from Baseline to Week 24)

| | |
|-----------------|---|
| End point title | Percent Change in TC/HDL-C ratio from Baseline at All Other Time Points to Week 104 (efficacy phase results from Baseline to Week 24) |
|-----------------|---|

End point description:

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

End point timeframe:

Percent Change in TC/HDL-C ratio from Baseline at All Other Time Points to Week 104 (refer also to the below-listed results covering the safety phase)

| End point values | All age groups | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 | 0.108 (± 27.5756) | | | |
| Week 8 | -5.292 (± 29.1737) | | | |
| Week 12 | -14.501 (± 27.7248) | | | |
| Week 16 | -33.384 (± 25.8765) | | | |
| Week 20 | -45.689 (± 27.0372) | | | |
| Week 24 | -52.155 (± 25.1906) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in TC/HDL-C ratio from Baseline at All Other Time Points to Week 104 (safety phase results from Week 28 to Week 104)

| | |
|-----------------|---|
| End point title | Percent Change in TC/HDL-C ratio from Baseline at All Other Time Points to Week 104 (safety phase results from Week 28 to Week 104) |
|-----------------|---|

End point description:

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

End point timeframe:

Percent Change in TC/HDL-C ratio from Baseline at All Other Time Points to Week 104 (refer also to the above-listed results covering the efficacy phase)

| End point values | All age groups | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 28 | -50.986 (± 31.0715) | | | |
| Week 32 | -48.651 (± 35.4572) | | | |
| Week 36 | -35.860 (± 35.4801) | | | |
| Week 40 | -43.976 (± 36.8573) | | | |
| Week 44 | -40.395 (± 38.1876) | | | |
| Week 48 | -41.720 (± 36.2674) | | | |
| Week 52 | -43.496 (± 38.2302) | | | |
| Week 56 | -39.188 (± 55.5616) | | | |
| Week 68 | -36.874 (± 41.9020) | | | |
| Week 80 | -39.189 (± 37.9268) | | | |
| Week 92 | -37.274 (± 41.0451) | | | |
| Week 104 | -39.358 (± 34.3438) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in HDL-C ratio from Baseline at All Other Time Points to Week 104 (efficacy phase results from Baseline to Week 24)

| | |
|-----------------|--|
| End point title | Percent Change in HDL-C ratio from Baseline at All Other Time Points to Week 104 (efficacy phase results from Baseline to Week 24) |
|-----------------|--|

End point description:

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

End point timeframe:

Percent Change in HDL-C ratio from Baseline at All Other Time Points to Week 104 (refer also to the below-listed results covering the safety phase)

| End point values | All age groups | | | |
|--------------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 | 1.428 (± 19.6280) | | | |
| Week 8 | 4.482 (± 26.0635) | | | |
| Week 12 | 4.912 (± 29.1215) | | | |
| Week 16 | 8.059 (± 31.4604) | | | |
| Week 20 | 6.186 (± 33.3664) | | | |
| Week 24 | 11.412 (± 33.0044) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in HDL-C ratio from Baseline at All Other Time Points to Week 104 (safety phase results from Week 28 to Week 104)

| | |
|-----------------|--|
| End point title | Percent Change in HDL-C ratio from Baseline at All Other Time Points to Week 104 (safety phase results from Week 28 to Week 104) |
|-----------------|--|

End point description:

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

End point timeframe:

Percent Change in HDL-C ratio from Baseline at All Other Time Points to Week 104 (refer also to the above-listed results covering the efficacy phase)

| End point values | All age groups | | | |
|--------------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 28 | 11.154 (± 36.3133) | | | |
| Week 32 | 15.137 (± 33.9304) | | | |
| Week 36 | 8.537 (± 30.2218) | | | |
| Week 40 | 10.043 (± 35.0097) | | | |
| Week 44 | 12.765 (± 33.2136) | | | |
| Week 48 | 13.602 (± 37.5732) | | | |
| Week 52 | 18.032 (± 35.1079) | | | |
| Week 56 | 11.528 (± 29.1750) | | | |
| Week 68 | 9.557 (± 30.6616) | | | |
| Week 80 | 11.606 (± 30.8242) | | | |
| Week 92 | 17.320 (± 33.0024) | | | |
| Week 104 | 16.109 (± 37.2987) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in LLT from Week 28 through Week 104

| | |
|-----------------|---|
| End point title | Change in LLT from Week 28 through Week 104 |
|-----------------|---|

End point description:

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

End point timeframe:

Week 28 through Week 104

| | | | | |
|--|-----------------|--|--|--|
| End point values | All age groups | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: Number of patients | | | | |
| Reduction due to low LDL-C | 2 | | | |
| Discontinuation due to lomitapide increase | 1 | | | |
| Discontinuation due to other reason | 2 | | | |
| Increase due to high LDL-C | 3 | | | |
| Increase due to other reason | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in LA from Week 28 through Week 104

| | |
|--------------------------|--|
| End point title | Change in LA from Week 28 through Week 104 |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Week 28 through Week 104 | |

| | | | | |
|-------------------------------------|-----------------|--|--|--|
| End point values | All age groups | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 17 | | | |
| Units: Number of patients | | | | |
| Reduction due to AE | 1 | | | |
| Reduction due to low LDL-C | 3 | | | |
| Reduction due to other reason | 4 | | | |
| Discontinuation due to low LDL-C | 1 | | | |
| Discontinuation due to other reason | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients Achieving EAS Recommended Target (2013) of LDL-C at any timepoint between Baseline and Week 24

| | |
|-----------------|---|
| End point title | Percentage of Patients Achieving EAS Recommended Target |
|-----------------|---|

(2013) of LDL-C at any timepoint between Baseline and Week 24

End point description:

End point type Secondary

End point timeframe:

Anytime up to Week 24

| End point values | All age groups | | | |
|------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: Percentage of patients | | | | |
| <135 mg/dL - anytime up to Week 24 | 42 | | | |
| <115 mg/dL - anytime up to Week 24 | 37 | | | |
| <110 mg/dL - anytime up to Week 24 | 33 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients Achieving EAS Recommended Target (2013) of LDL-C at any time in the study

End point title Percentage of Patients Achieving EAS Recommended Target (2013) of LDL-C at any time in the study

End point description:

End point type Secondary

End point timeframe:

Anytime in the study

| End point values | All age groups | | | |
|-------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: Percentage of patients | | | | |
| <135 mg/dL - anytime up to week 104 | 54 | | | |
| <115 mg/dL - anytime up to week 104 | 57 | | | |
| <110 mg/dL - anytime up to week 104 | 44 | | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percent change of BMI (efficacy phase results from Baseline to Week 24)

| | |
|-----------------|---|
| End point title | Percent change of BMI (efficacy phase results from Baseline to Week 24) |
|-----------------|---|

End point description:

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Baseline to Week 104 (refer also to the data presented in the table below for the safety phase)

| End point values | All age groups | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 | -1.06 (± 3.466) | | | |
| Week 8 | -1.32 (± 3.954) | | | |
| Week 12 | -2.36 (± 4.768) | | | |
| Week 16 | -2.96 (± 5.288) | | | |
| Week 20 | -4.21 (± 5.708) | | | |
| Week 24 | -5.04 (± 5.997) | | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percent change of BMI (safety phase results from Week 28 to Week 104)

| | |
|-----------------|---|
| End point title | Percent change of BMI (safety phase results from Week 28 to Week 104) |
|-----------------|---|

End point description:

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Baseline to Week 104 (refer also to the data presented in the table above for the efficacy phase)

| End point values | All age groups | | | |
|--------------------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 28 | -4.13 (± 6.427) | | | |
| Week 32 | -3.60 (± 7.145) | | | |
| Week 36 | -3.92 (± 7.949) | | | |
| Week 40 | -3.78 (± 8.293) | | | |
| Week 44 | -3.71 (± 10.406) | | | |
| Week 48 | -3.92 (± 10.420) | | | |
| Week 52 | -3.21 (± 10.738) | | | |
| Week 56 | -2.90 (± 11.520) | | | |
| Week 68 | -3.00 (± 12.103) | | | |
| Week 80 | -1.90 (± 12.665) | | | |
| Week 92 | -1.00 (± 14.108) | | | |
| Week 104 | -0.11 (± 13.718) | | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Lipid Accumulation in the Liver Over Time - NMR (efficacy phase results from Baseline to Week 24)

| | |
|-----------------|---|
| End point title | Lipid Accumulation in the Liver Over Time - NMR (efficacy phase results from Baseline to Week 24) |
|-----------------|---|

End point description:

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

From Baseline to Week 104/EoT. Please refer also to the data below for data from the safety phase.

| End point values | 5-10 years | 11-17 years | | |
|------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 4 | 19 | | |
| Units: Number of patients | | | | |
| Baseline - ≤10% liver fat | 2 | 16 | | |
| Baseline - >10% and ≤20% liver fat | 0 | 1 | | |

| | | | | |
|-----------------------------------|---|----|--|--|
| Baseline - >20% liver fat | 0 | 0 | | |
| Week 24 - ≤10% liver fat | 1 | 12 | | |
| Week 24 - >10% and ≤20% liver fat | 1 | 2 | | |
| Week 24 - >20% liver fat | 0 | 1 | | |
| Week 24 - No result | 2 | 4 | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Lipid Accumulation in the Liver Over Time - NMR (safety phase results from Week 28 to Week 104)

| | |
|-----------------|---|
| End point title | Lipid Accumulation in the Liver Over Time - NMR (safety phase results from Week 28 to Week 104) |
|-----------------|---|

End point description:

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

From Baseline to Week 104/EoT. Please refer also to the data above for data from the efficacy phase.

| End point values | 5-10 years | 11-17 years | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 4 | 19 | | |
| Units: Number of patients | | | | |
| Week 56 - ≤10% liver fat | 0 | 9 | | |
| Week 56 - >10% and ≤20% liver fat | 1 | 4 | | |
| Week 56 - >20% liver fat | 0 | 0 | | |
| Week 56 - No result | 2 | 5 | | |
| Week 104/EoT - ≤10% liver fat | 3 | 11 | | |
| Week 104/EoT - >10% and ≤20% liver fat | 1 | 4 | | |
| Week 104/EoT - >20% liver fat | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Lipid Accumulation in the Liver Over Time - Ultrasound (efficacy phase results from Baseline to Week 24)

| | |
|-----------------|--|
| End point title | Lipid Accumulation in the Liver Over Time - Ultrasound (efficacy phase results from Baseline to Week 24) |
|-----------------|--|

End point description:

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

From Baseline to Week 104/EoT. Please refer also to the data below for data from the safety phase.

| End point values | 5-10 years | 11-17 years | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 2 | | |
| Units: Number of patients | | | | |
| Baseline - $\leq 10\%$ liver fat | 17 | 2 | | |
| Baseline - $> 10\%$ and $\leq 20\%$ liver fat | 0 | 0 | | |
| Baseline - $> 20\%$ liver fat | 0 | 0 | | |
| Week 24 - $\leq 10\%$ liver fat | 15 | 2 | | |
| Week 24 - $> 10\%$ and $\leq 20\%$ liver fat | 0 | 0 | | |
| Week 24 - $> 20\%$ liver fat | 0 | 0 | | |
| Week 24 - No result | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Lipid Accumulation in the Liver Over Time - Ultrasound (safety phase results from Week 28 to Week 104)

| | |
|-----------------|--|
| End point title | Lipid Accumulation in the Liver Over Time - Ultrasound (safety phase results from Week 28 to Week 104) |
|-----------------|--|

End point description:

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

From Baseline to Week 104/EoT. Please refer also to the data above for data from the efficacy phase.

| End point values | 5-10 years | 11-17 years | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 2 | | |
| Units: Number of patients | | | | |
| Week 56 - $\leq 10\%$ liver fat | 15 | 2 | | |
| Week 56 - $> 10\%$ and $\leq 20\%$ liver fat | 1 | 0 | | |
| Week 56 - $> 20\%$ liver fat | 0 | 0 | | |
| Week 56 - No result | 0 | 0 | | |
| Week 104/EoT - $\leq 10\%$ liver fat | 15 | 0 | | |
| Week 104/EoT - $> 10\%$ and $\leq 20\%$ liver | 0 | 1 | | |
| Week 104/EoT - $> 20\%$ liver fat | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were monitored throughout the study from the time of informed consent through Week 108.

Adverse event reporting additional description:

Safety variables included evaluations of AEs, laboratory test results (including assessment of bone health), vital signs, ECGs, pulmonary function tests, and imaging of the liver. In addition, available standard of care echocardiography results were reviewed.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 27.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | All patients |
|-----------------------|--------------|

Reporting group description:

All patients from all age groups from the time of informed consent through Week 108.

| Serious adverse events | All patients | | |
|---|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 11 / 43 (25.58%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | 0 | | |
| Investigations | | | |
| Transaminases increased | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Arteriovenous fistula thrombosis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Shunt occlusion | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subdural haematoma | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Aortic arteriosclerosis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Aortic valve disease mixed | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Vascular device occlusion | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Tendon disorder | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Vascular device infection | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Septic shock | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| 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 | All patients | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 42 / 43 (97.67%) | | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 17 / 43 (39.53%) | | |
| occurrences (all) | 28 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 15 / 43 (34.88%) | | |
| occurrences (all) | 28 | | |

| | | | |
|--|------------------|--|--|
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 6 / 43 (13.95%) | | |
| occurrences (all) | 6 | | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 6 / 43 (13.95%) | | |
| occurrences (all) | 8 | | |
| ECG signs of ventricular hypertrophy | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | | |
| occurrences (all) | 5 | | |
| Transaminases increased | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | | |
| occurrences (all) | 7 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 4 / 43 (9.30%) | | |
| occurrences (all) | 8 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 14 / 43 (32.56%) | | |
| occurrences (all) | 21 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 8 / 43 (18.60%) | | |
| occurrences (all) | 12 | | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 22 / 43 (51.16%) | | |
| occurrences (all) | 44 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 19 / 43 (44.19%) | | |
| occurrences (all) | 59 | | |
| Vomiting | | | |
| subjects affected / exposed | 12 / 43 (27.91%) | | |
| occurrences (all) | 26 | | |
| Abdominal pain upper | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 5 / 43 (11.63%) | | |
| occurrences (all) | 9 | | |
| Nausea | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | | |
| occurrences (all) | 6 | | |
| Flatulence | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | | |
| occurrences (all) | 3 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 7 / 43 (16.28%) | | |
| occurrences (all) | 9 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 4 / 43 (9.30%) | | |
| occurrences (all) | 6 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dry skin | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | | |
| occurrences (all) | 6 | | |
| Xanthoma | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | | |
| occurrences (all) | 4 | | |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 9 / 43 (20.93%) | | |
| occurrences (all) | 12 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 6 / 43 (13.95%) | | |
| occurrences (all) | 12 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 43 (9.30%) | | |
| occurrences (all) | 6 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | | |
| occurrences (all) | 3 | | |
| Pharyngitis | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 3 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 6 / 43 (13.95%) | | |
| occurrences (all) | 8 | | |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 4 / 43 (9.30%) | | |
| occurrences (all) | 4 | | |
| Abnormal loss of weight | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | | |
| occurrences (all) | 3 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 18 August 2019 | Amendment 1.0: <ul style="list-style-type: none">- Inconsistencies between the timing of assessments in the study flowchart and the visit descriptions corrected.- Assessment of bone health as a secondary objective clarified.- Genetic testing procedure clarified.- Description of palatability assessments included. |
| 04 December 2019 | Amendment 2.0 (first version of protocol approved in Germany): <ul style="list-style-type: none">- Change of exclusion criterion 12 to avoid overlapping toxicities.- Amendment of exclusion criterion 14 to exclude breastfeeding subjects from the study.- Change of subject discontinuation criteria to obligatory permanently discontinue treatment in subjects meeting Hy's law case criteria or showing any comparable signs of liver toxicity, irrespective of origin.- Implementation of recruitment stop and individual benefit risk assessment for further administration of study medication in case a subject must discontinue treatment due to Hy's law or comparable signs of liver toxicity. |
| 14 February 2020 | Amendment 3.0 (Amendment 1.0 in Germany): <ul style="list-style-type: none">- Long-term extension phase of study added instead of named patient supply of lomitapide.- Permission to down-titrate to intermediate doses at Investigator's discretion added.- Central laboratory measurements of fat-soluble vitamin levels and EFAs added.- Central genetic testing added and clarified that genetic testing was to be strongly encouraged but not mandated.- Exploratory sub-study (Liposcale® Test) using aliquots of PK samples added.- Screening laboratory tests for HBsAg and hepatitis C antibody deleted.- Inconsistencies between study flowchart and visit schedule for serum lipase corrected.- Address for SAE reporting updated.- Inconsistencies in safety follow-up and safety reporting details corrected.- Parameters to be measured during pulmonary function tests clarified.- Procedure for weighing subjects clarified.- Study design figure simplified.- Updated to allow local sourcing of dietary supplements.- List of participating countries revised. |
| 04 September 2020 | Amendment 4.0: <ul style="list-style-type: none">- Inconsistencies in safety follow-up and safety reporting details corrected in Amendment 3.0 reverted (at request of BfArM, Germany).- Use of MRI or ultrasound for measurement of lipid accumulation in the liver clarified.- Rationale for dose selection updated.- Assessment of vital signs at every visit and inclusion of ECGs every 3 to 6 months added.- Collection of standard-of-care echocardiography data/results when available added.- Contraceptive measures section updated.- Re-screening process clarified.- Measurement of 'Holman Index' i.e., ratio of eicosatrienoic acid to arachidonic acid removed.- Sponsor address updated. |

| | |
|-------------------|--|
| 21 September 2020 | Amendment 4.1: - Inconsistency in flowchart footnotes corrected. |
| 17 November 2020 | Amendment 4.2 (implemented in Germany only): - Re-screening details updated (at request of BfArM, Germany). |
| 05 May 2022 | Amendment 5.0: - Inconsistencies between objectives and endpoints corrected. - Updated to allow dose increase after Week 24. - Statistical methods clarified: - Clarified methodology of primary efficacy analysis and added timing of the primary efficacy analysis and final analysis. - Specified the use of 2-side significance level at 5% for primary and secondary efficacy parameters. - Updated definition of study population to clarify that safety analysis set included subjects with least one dose of the study medication, FAS included subjects with at least one post-Baseline measurement of LDL-C and completers analysis set included subjects not discontinued at the end of efficacy phase. - Analysis of primary efficacy endpoint was updated to specify the use of one sample t test to test the primary efficacy endpoint, clarified that imputation of missing data using LOCF only applies to Efficacy Phase and when a Baseline value is not missing, added sensitivity analyses using a MMRM, supplementary analyses based on per-protocol and completers analysis sets and subgroup analyses. - Addition of visit windows to handle time window violations for lipid data analyses. - Addition of exploratory and palatability endpoints. - Use of PER Registry for subjects who became pregnant during the study removed. |
| 09 February 2023 | Amendment 6.0: - Updated to remove reference to long-term extension study and include options to enter an EAP for subjects <18 years of age or to transition to commercial product for subjects ≥18 years of age. - References to EMA SmPC updated to Lojuxta® SPC in lieu of an Investigator's Brochure. - Updated to remove PK analysis of lomitapide metabolites. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Lp(a) analysis was analysed locally as central analysis was only available from January 2022.

Notes: